

EXPOSURE TO URBANIZATION AND ITS LONGITUDINAL ASSOCIATION WITH BLOOD AND PULSE  
PRESSURE IN ADULT FILIPINO WOMEN

Alberto Vargas

A thesis submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of  
the requirements for the degree of Master of Science in the Department of Nutrition in the Gillings  
School of Global Public Health.

Chapel Hill  
2017

Approved by:

Linda S. Adair

Elizabeth Mayer-Davis

Sandra Albrecht

©2017  
Alberto Vargas  
ALL RIGHTS RESERVED

## **ABSTRACT**

Alberto Vargas: Exposure to Urbanization and its Longitudinal Association with Blood and Pulse Pressure  
in Adult Filipino Women  
(Under the direction of Linda Adair)

Urbanization may adversely affect blood (BP) and pulse pressures (PP) as individuals migrate or as their surroundings urbanize. We determined how urbanicity (UI) is associated with BP and PP in adult women of the Cebu Longitudinal Health and Nutrition Survey (CLHNS) from 1998-2012.

We identified participants (N=2107) as movers and non-movers. The former moved between communities between survey years (1998, 2002, 2005, and 2012). We estimated mixed-effects longitudinal regression models of the change in UI-change in SBP, DBP, and PP relationships.

Movers' UI increased more than non-movers' throughout follow-up. Change in UI effected change in SBP, DBP, and PP differently according to previous UI. Moving effected change in SBP, DBP, but not PP, differently according to previous UI.

Predicted BP and PP was highest among previous rural dwellers who underwent UI increases and the oldest participants, respectively. Special attention should be paid to young and migrating populations.

## TABLE OF CONTENTS

LIST OF TABLES.....	v
LIST OF FIGURES.....	vi
LIST OF ABBREVIATIONS .....	vii
CHAPTER 1-URBANICITY AND BLOOD PRESSURE IN THE PHILIPPINES .....	1
Background .....	1
Methods .....	3
Study Variables .....	3
Statistical Analyses .....	6
Results .....	9
Changes and Secular trends in BP, PP, and UI .....	11
Change in BP models .....	11
Medication model .....	22
Mortality Outcome Models .....	23
CHAPTER 2-DISCUSSION AND SYNTHESIS.....	24
Overview of Major Findings.....	24
Comparison with Previous Literature .....	25
Limitations and Strengths .....	27
Public Health Implications and Conclusions .....	28
APPENDIX 1: ADDITIONAL RESULTS.....	30
REFERENCES.....	37

## LIST OF TABLES

TABLE 1 - Demographic characteristics of a longitudinal cohort of eligible participants in the Philippines in 1998 .....	10
TABLE 2 - Final Change in BP by change in UI model results output .....	21
TABLE 3 - Full medication model results output .....	22
TABLE 4 – Mortality outcome model results .....	23
SUPPLEMENTAL TABLE 1 - Correlation matrix of household asset variables included in household wealth score .....	30
SUPPLEMENTAL TABLE 1.1 - Notation key for SUPPLEMENTAL TABLES 2-5 .....	31
SUPPLEMENTAL TABLE 2 - Characteristics of a Longitudinal Cohort of Eligible Adult Filipino Women Participants from 1998-2012 .....	32
SUPPLEMENTAL TABLE 3 - Characteristics of a Longitudinal Cohort of Eligible Adult Filipino Women Participants by Moving Status 1998-2012 .....	33
SUPPLEMENTAL TABLE 4 - Longitudinal Characteristics of Non-Movers by Direction of Urbanization from 1998-2012 .....	34
SUPPLEMENTAL TABLE 5 - Longitudinal Characteristics of Movers by Direction of Urbanization from 1998-2012 .....	35

## LIST OF FIGURES

FIGURE 1 - Directed Acyclic Graph of the Relationship between change change in UI and change in BP and PP .....	8
FIGURE 2 - Mean systolic and diastolic blood pressure of CLHNS women by survey year .....	12
FIGURE 3 - Observed secular trends in SBP and DBP from 1998-2012 stratified by baseline age groups .....	13
FIGURE 4 - Observed median Urbanicity Index* by survey year, moving patterns, and direction of urbanization .....	14
FIGURE 5 - Predicted change in SBP by change in UI across previous UI .....	16
FIGURE 6 - Predicted change in SBP by change in UI and age .....	16
FIGURE 7 - Predicted change in DBP by change in UI across previous UI Adult Filipino Women Participants from 1998-2012 .....	18
FIGURE 8 - Predicted change in DBP by change in UI across age Adult Filipino Women Participants by Moving Status 1998-2012 .....	18
FIGURE 9 - Predicted change in PP by change in UI previous UI Direction of Urbanization from 1998-2012 .....	20
FIGURE 10 - Predicted change in PP by change in UI across age Direction of Urbanization from 1998-2012 .....	20
SUPPLEMENTAL FIGURE 1 - Observed secular trends in SBP and DBP from 1998-2012 by baseline age groups among participants with full participation .....	36

## LIST OF ABBREVIATIONS

24-HR	24-hour Recall
BMI	Body-Mass Index
BP	Blood Pressure
CLHNS	Cebu Longitudinal Health and Nutrition Survey
CM	Cardiometabolic
CMD	Cardiometabolic Disease
CVD	Cardiovascular Disease
DAG	Directed Acyclic Graph
DBP	Diastolic Blood Pressure
FCT	Food Composition Table
IWI	International Wealth Index
LMIC	Low and Middle Income Countries
NNS	National Nutrition Survey
PP	Pulse Pressure
SBP	Systolic Blood Pressure
SES	Socioeconomic Status
UI	Urbanicity Index
WC	Waist Circumference

## **CHAPTER 1: URBANICITY AND BLOOD PRESSURE IN THE PHILIPPINES**

### **Background**

Living in urban environments may adversely affect health by promoting poor dietary habits, physical inactivity, and cigarette smoking in low and middle income countries (LMICs). Together, these behaviors contribute to the burden of chronic diseases such as obesity, diabetes, and hypertension, increasingly seen in LMICs undergoing the nutrition transition. On the other hand, urbanization may also improve health by increasing availability and accessibility of health care, and by providing centralized services such as piped water. While the higher socioeconomic status (SES) associated with greater urbanization may partially mitigate the burden of obesity and hypertension, obesity is still more prevalent among the most affluent in LMICs, but the burden is now shifting to the poorest.

The Philippines exemplifies many of the changes associated with the nutrition transition<sup>1</sup>, including increasing rates of obesity and cardiovascular diseases. Previous research from the Cebu Longitudinal Health and Nutrition Survey (CLHNS) found that the risk for hypertension is twice as high among overweight compared to normal or underweight weight Filipino women<sup>2</sup>. In addition, the risk for stage II hypertension (Systolic Blood Pressure  $\geq 160$  or DBP  $\geq 100$ ) is more than twice as high among those with abdominal obesity (Waist-to-hip Ratio  $>0.85$ ) compared with those with normal abdominal adiposity<sup>2</sup>. Trends in blood pressure status among Filipino adults aged  $>20$ y from the nationally representative Philippine National Nutrition Survey (NNS) show that hypertension has been prevalent in 1 in 5 adults since 2003.<sup>3,4</sup>

Hypertension may be prevalent in both the affluent and the poor and in urban and rural communities. In the Philippines, higher rates of obesity and central adiposity may dominate as risk factors for



hypertension among higher SES, more urban populations, but excessive sodium consumption associated with poverty diets may dominate among the rural poor.

Dietary and environmental exposures associated with urbanization and modernization may be key risk factors in the development and progression of hypertension as individuals are exposed to urban environments due to abrupt migration into more urban places or as their surroundings urbanize over time. **Yet, we know little about how exposure to urban environments impacts CM health in populations with different history of exposure to urban environments. Specifically, it is not yet clear how exposure to urban environments relates to SBP and DBP separately despite the current medically relevant individual SBP and DBP cutoff values used to define different BP status categories.**

Furthermore, the relationship between urbanicity and pulse pressure (PP) has never been explored despite this parameter being considered as a significant independent predictor of stroke and myocardial infarction among middle-aged and older adults.<sup>5-8</sup>

**The current study aims to determine how exposure to urban environments is associated with systolic and diastolic blood pressure in a cohort of adult Filipino women from the CLHNS.** This cohort is important to study due to higher CMD risk found in Asian populations at lower BMI levels compared with Caucasians<sup>39</sup>. The Philippines is an important site for this research due to its rapid urbanization and socioeconomic development since the advent of the CLHNS in 1983.

To address current gaps in the literature, we will (1) describe CLHNS participants' exposure to urbanicity and their patterns of SBP, DBP, and PP across four survey rounds (1998, 2002, 2005, and 2012), (2) classify exposure to urbanicity into two mutually exclusive groups comprised of those who moved to different communities between survey rounds and those who remained in the same communities between survey rounds, and (3) estimate the longitudinal association between change in urbanicity and changes in SBP, DBP, and PP (separately) among CLHNS mothers from 1998 to 2012, and

determine whether abrupt changes related to moving to a different community vs gradual change related to increasing urbanization *in situ* relate differently to BP.

## **Methods**

Data were derived from the CLHNS, a community based survey that initially enrolled 3,327 pregnant women from 33 randomly selected urban and rural barangays (administrative units, that are communities in urban areas or villages in rural areas) of Metro Cebu. The CLHNS has followed these women since 1983<sup>31</sup>. The study includes high quality information on barangay characteristics that describe population size and density, communication and health services, metropolitan transportation, and types and number of markets for >150 barangays measured over time. BP and waist circumference (WC) were first measured in 1998 and 1994, respectively. We have >10 years of BP and anthropometric measurements. In addition, we have detailed migration history information. We include women who participated in 4 survey rounds from 1998 to 2012 (1998, 2002, 2005, and 2012). Our final analytic sample includes 2107 non-pregnant women aged 29-62 y in 1998, with complete BP, anthropometric, diet, and select demographic data for at least 1 survey year. Women in our sample had 2.7 observations on average through the follow-up period.

### Study Variables

#### ***Blood pressure***

From 1998 to 2005, BP was measured in triplicate after a 10-minute seated rest using mercury sphygmomanometers. After recommendations to cease use of mercury instruments, the 2012 survey used OMRAN digital BP devices. A subsample was assessed using the new and old instruments to assess comparability of measurement methods. Hypertension is defined per the International Diabetes Federation cutoffs (SBP >130 and/or diastolic > 85 mm Hg or taking hypertension medication).<sup>9</sup> PP was calculated as the difference between SBP and DBP.

## **Mortality**

Cause-specific mortality data were collected both in 2005 and 2012 based on available family members' report of cause of death. Review of a subset of cases with available death certificate data indicated high agreement of family-reported and formally reported cause of death. For our interest, we grouped mortality by 'hypertension', 'heart disease', and 'combination of hypertension and diabetes' in a single binary variable denoted as 'hypertension-related mortality' (yes/no).

## **Anthropometry**

Height, weight, and WC and hip circumferences were measured in the home using standard protocols. Weight status was categorized for some analyses using BMI and waist circumference (WC) cutpoints recommended for Asians (overweight=BMI>23, obese=BMI>27.5 kg/m<sup>2</sup>, and high WC (WC ≥80 cm).<sup>10-13</sup>

## **Diet**

Diet was assessed by use of 24-hour recalls (24-HR). We used 1 day of recall for the years where there were two recalls to be consistent with the 1998 survey which only has one recall. We use the Philippines Food Composition Table (FCT) produced by the Food and Nutrition Research Institute of the Philippines (FNRI) to estimate nutrient intake in each participant.<sup>14</sup> We estimate and compare trends in energy intake through our follow-up period.

## **Sociodemographic Characteristics**

### **Age**

Age was calculated based on the time between the interview date and the birthdate of participants. Non-linear relationships between age and primary outcomes were assessed.

### **Socioeconomic Status**

We included log household income per capita, education level, and a household wealth index score as key SES characteristics in the population. Education level was based on the participant's self-

reported highest attained education level and categorized as completion of primary (6<sup>th</sup> grade or less), secondary (7<sup>th</sup>-12<sup>th</sup> grade), or above high school education. We used principal components analysis to construct a household wealth index variable. The index sought the set of factors to account for all of the common and unique variance in a set of household asset variables. The specific types and number of variables included were based on the International Wealth Index (IWI), an asset-based index of household's material well-being or economic status apt to be used in LMICs.<sup>15</sup> We modified the list of assets from the IWI based on available household-level characteristics assessed during the 1994 CLHNS household survey round by trained interviewers. Household asset data includes ownership of consumer durables (e.g. television, refrigerator, bicycle, etc.), housing characteristics (e.g. quality of floor material, toilet facilities, number of rooms, etc.), access to electricity, source of drinking water, and cooking fuel. For a complete list of household assets and their correlation matrix, refer to **supplemental table 1**.

### **Migration**

The CLHNS collected a detailed migration history at each survey. Participants were asked whether they had moved since their previous survey participation, and to identify all barangays in which they had resided. Movers were considered as those who moved between barangays. Migrants who left the Metro Cebu area were not followed.

### **Urbanization**

Community data were collected from all barangays in Metro Cebu where respondents resided at the time of each survey. Community surveys were conducted with key informants, supplemented with census data. A multicomponent urbanicity index (UI), based on community surveys in each survey year<sup>16</sup>, reflects population size and density, community infrastructure, economic and environment characteristics. UI scores range from 0-70 where greater levels imply more urban characteristics. We calculated the change in UI experienced by each participant between each survey year and considered it as our primary exposure of interest.

## Final Sample

Our analytic sample includes 5614 observations from 2107 non-pregnant women aged ~29-62 y in 1998, with complete UI, blood pressure, and select demographic data. Women pregnant at the time of the survey were excluded from the analysis only for the year in which they were pregnant. Not all mothers were present in every survey year. The mean number of surveys for each women 2.7.

## Statistical Analyses

To examine the relationship between change in UI and BP, we estimated a series of mixed-effects longitudinal and cross-sectional models. For each outcome (SBP, DBP and PP), we modeled both initial levels and between survey change in UI, and moving as main exposures. We used a directed acyclic graph (DAG) to determine relevant confounders. Our minimally adjusted sets include age and SES variables (education level, log income per capita, and household wealth score) as confounders. Our DAG (**fig. 1**) shows that diet, occupational physical activity, WC, smoking status, alcohol intake, and medication use as possible mediators of the change in UI- change in BP relationship. Once confounders were identified, we tested the possibility of heterogeneity of effects of (1) change in UI on change in BP and PP across levels of previous UI (to determine whether changes in UI related differently to BP and PP according to the initial level of UI); (2) moving on changes in BP and PP across levels of lagged UI (to determine whether changes in UI had different effects on BP and PP depending on whether the change was related to moving to a different barangay or urbanization in situ; and (3) change in UI on change in PP across age (to determine whether changing UI had different effects on PP on younger vs older women). We assessed non-linear relationships using squared and cubic age terms. We also tested non-linear relationships of BP and PP with other continuous variables by categorizing into quantiles, evenly spaced categories, squared and cubic terms, and spline knots; considering ease of interpretability of category choices. To aid in the interpretation of interaction terms, we conducted simulations based on

conditioning of sample characteristics to predict changes in BP and PP. Explanations for each simulation are based on the regression equation below:

$$\text{Predicted value} = \beta_0 + \beta_1 X_1 + \beta_2 X_{2, \text{year}} + \beta_3 X_3 + \beta_4 X_3 X_1 + \beta_5 X_4 + \beta_6 X_4 X_3 + \beta_7 X_{5, Q_i \text{wealth}} + \beta_8 X_6 + \beta_9 X_6 X_1 + \beta_{10} X_6^2 + \beta_{11} X_6^2 X_1 + \beta_{12} X_6^3 + \beta_{13} X_6^3 X_1 + \epsilon$$

Where:

$X_1$  = Change in UI

$X_2$  = Survey Year (2005 and 2012 compared to 2002)

$X_3$  = Previous UI

$X_3 X_1$  = Change in UI-Previous UI interaction

$X_4$  = Moving (non-mover, movers)

$X_4 X_3$  = Moving-Previous UI interaction

$X_5$  = Lagged wealth score quintile

$X_6^n$  = Age to the n power

$\epsilon$  = Error term

$\beta_0$  = Constant value when  $X_i = 0$

$\beta_1$  = Change in expected outcome per unit changes in UI

$\beta_2$  = Change in expected outcome by survey year (2002, 2005, and 2012)  $\beta_3$  = Change in expected outcome per unit changes in previous UI

$\beta_4$  = Change in expected outcome by change in UI-previous UI interaction (increases in slope due to increments in previous UI

$\beta_5$  = Change in expected outcome by moving

$\beta_6$  = Change in expected outcome by moving-previous UI interaction (increases in previous UI slope due to moving)

$\beta_7$  = Change in expected outcome by quintile of wealth score compared to 1<sup>st</sup> quintile.

$\beta_8$  = Change in expected outcome per unit changes in age

$\beta_9$  = Change in expected outcome by age-change in UI interaction (changes in age slope due to changes in UI)

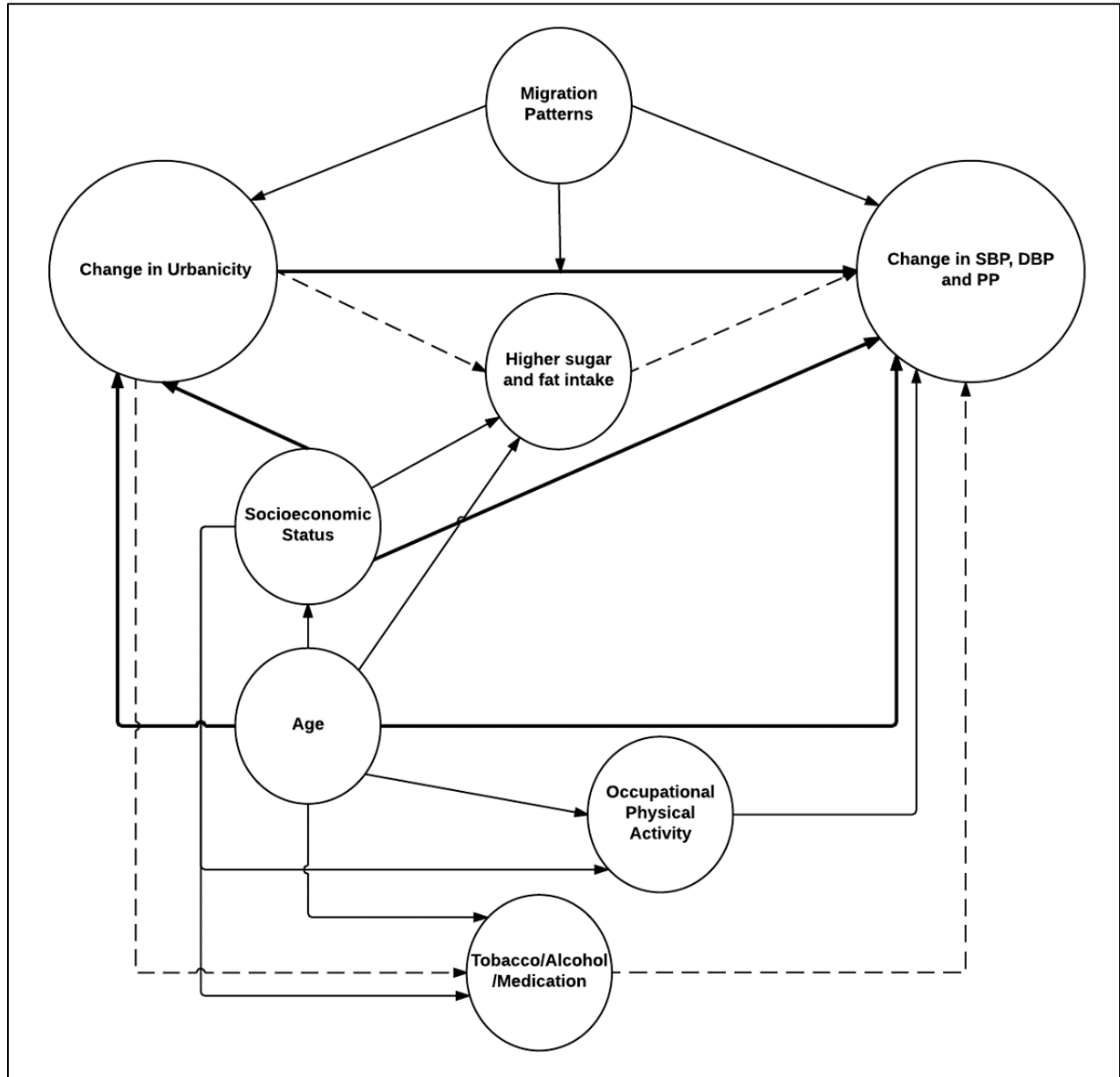
$\beta_{10}$  = Change in expected outcome per unit changes in squared age

$\beta_{11}$  = Change in expected outcome by squared age-change in UI interaction (changes in squared age slope due to changes in UI)

$\beta_{12}$  = Change in expected outcome per unit changes in cubic age

$\beta_{13}$  = Change in expected outcome by cubic age-change in UI interaction (changes in cubic age slope due to changes in UI

**FIGURE 1. Directed Acyclic Graph\* of the Relationship between change in UI† and change in BP and PP‡**



\***Bolded and dashed lines represent the confounding and mediating pathways in the change in UI-change in BP relationship, respectively.**

†Denotes changes in Urbanicity Index score between survey rounds.

‡Blood pressure was measured from 1998 in triplicate after a 10-minute seated rest using mercury sphygmomanometers. Means were derived from the average of three BP measurements. Pulse Pressure was derived from the difference between systolic and diastolic blood pressures.

Medication use was not included in the BP models because we considered medication use to be in the pathway between change in UI and change in BP/PP, implying that changes in UI may precede medication use in our sample. Given how medication artificially lowers BP, adjusting for it in our models may attenuate the net effect of change in UI on our outcomes. Instead, to explore the role of medication use in the UI-BP relationship, we estimated the association of change in UI and moving with the likelihood of using anti-hypertensive medication among participants with hypertension based on IDF cutoffs (SBP/DBP > 130/85).<sup>9</sup> Our final **medication model** include change in UI, squared change in UI, moving, age, survey year, and previous wealth quintiles. Models were estimated with mixed-effect longitudinal logistic regressions.

Finally, to determine the potential public health significance of the effect sizes observed in the analysis models, we assessed the relationship of SBP, DBP, and PP in 2005, separately, with the likelihood of hypertension-related mortality between 2005 and 2012 (N= 36 deaths).

Statistical analyses were conducted using STATA version 13.0 (Stata Corporation, College Station, TX, 2006). Detailed final model specifications and results are described in **tables 2, 3, and 4**. We consistently used  $\alpha < 0.05$  and  $\alpha < 0.10$  as the criterion for statistical significance for main effects and interaction terms, respectively.

## Results

We describe sample characteristics among eligible participants from our longitudinal cohort in 1998 as well as characteristics by survey round (1998, 2002, 2005, and 2012) in **table 1 and supplemental table 2-5**, respectively. In 1998, on average, participants were >40 y, lived in barangays with UIs of ~39, and had SBPs and DBPs >113 and >76 mmHg, on average. Most participants attained a 6<sup>th</sup> grade or lower level of education and ~8.7% of the sample reported moving barangays from when these were last surveyed. Mean and median UI, SBP, PP, WC, BMI, log income per capita, percentage with 6<sup>th</sup> grade or lower education, and percentage movers were highest in 2012 (**Supp. Table 2**). In spite



of moving, mothers tended to experience increases in UI compared to no changes or decreases throughout the follow-up period (**Supp. Table 3**) However, in 2005 more participants experienced UI decreases compared to no changes or UI increases. In non-movers, the highest mean SBP, DBP, and PP observed was >135, >79, and >55 mmHg in 2012, respectively (**Supp. Table 4**). In movers, the highest BP and PP values were found in 2005 (**Supp. Table 5**).

<b>TABLE 1. Demographic characteristics of a longitudinal cohort of eligible participants in the Philippines in 1998*</b>	
<b>N†</b>	1938
<b>Age‡</b>	41.92 ± 0.14
<b>Urbanicity Index§</b>	38.95 ± 0.31
<b>Systolic Blood Pressure#</b>	113.45 ± 0.41
<b>Diastolic Blood Pressure**</b>	76.82 ± 0.27
<b>Pulse Pressure††</b>	36.63 ± 0.23
<b>Waist Circumference‡‡</b>	76.04 ± 0.21
<b>Body Mass Index§§</b>	23.65 ± 0.09
<b>Energy Intake##</b>	1268.58 ± 12.92
<b>Log Income per Capita***</b>	0.96 ± 0.01
<b>Education Level†††</b>	
<6th Grade	1094(56.45)
7th-12th Grade	560(28.9)
>High School Education	284(14.65)
<b>Migration Status†††</b>	
Non-Movers	1770(91.33)
Movers	168(8.67)
<b>Direction of Urbanization§§§</b>	
No change	132(6.81)
Positive	1399(72.19)
Negative	288(14.86)
Missing	119(6.14)

\*All data derived from the Cebu Longitudinal Health and Nutrition Survey (CLHNS) 1998, 2002, and 2005, and 2012 survey rounds. Our analytic sample includes 2107 participants aged 29-62 y in 1998 with complete blood pressure and select demographic data. Continuous and categorical variables are expressed as "mean ± S.E" and "count (percent)", respectively.

†Total number of participants interviewed in 1998.

‡Based on self-reported age as of last birthday.

§ Multicomponent index that represents a gradient from rural to urban. It is derived from community surveys each survey year that reflects population size and density, community infrastructure, economic and environmental characteristics. Increasing continuous amount represent higher urban characteristics.

# Blood pressure (BP) was measured from 1998 in triplicate after a 10-minute seated rest using mercury sphygmomanometers.

\*\* See #

††Calculated from the difference between Systolic and Diastolic Blood pressures.

‡‡ Measured by trained specialists.

§§ Height (m) and weight (kg) were measured at home by trained specialists using standardized methods.

## Estimated energy intake (kcal) in one 24-hr recall per survey round. We use conversion factors to account for moisture and fat retention due to cooking methods (e.g. boiling, braising, and frying).

\*\*\* Estimated weekly household income. Log transformation was performed due to income disparities in the Philippines.

††† Based on participant's self-reported highest attained education level. Participants who did not know or reported "N/A" were considered to not have completed a single grade.

††††Based on whether participants moved to different barangays between survey rounds.

§§§Based on whether participants experienced null, positive, or negative changes in UI.

## Changes and Secular trends in BP, PP, and UI

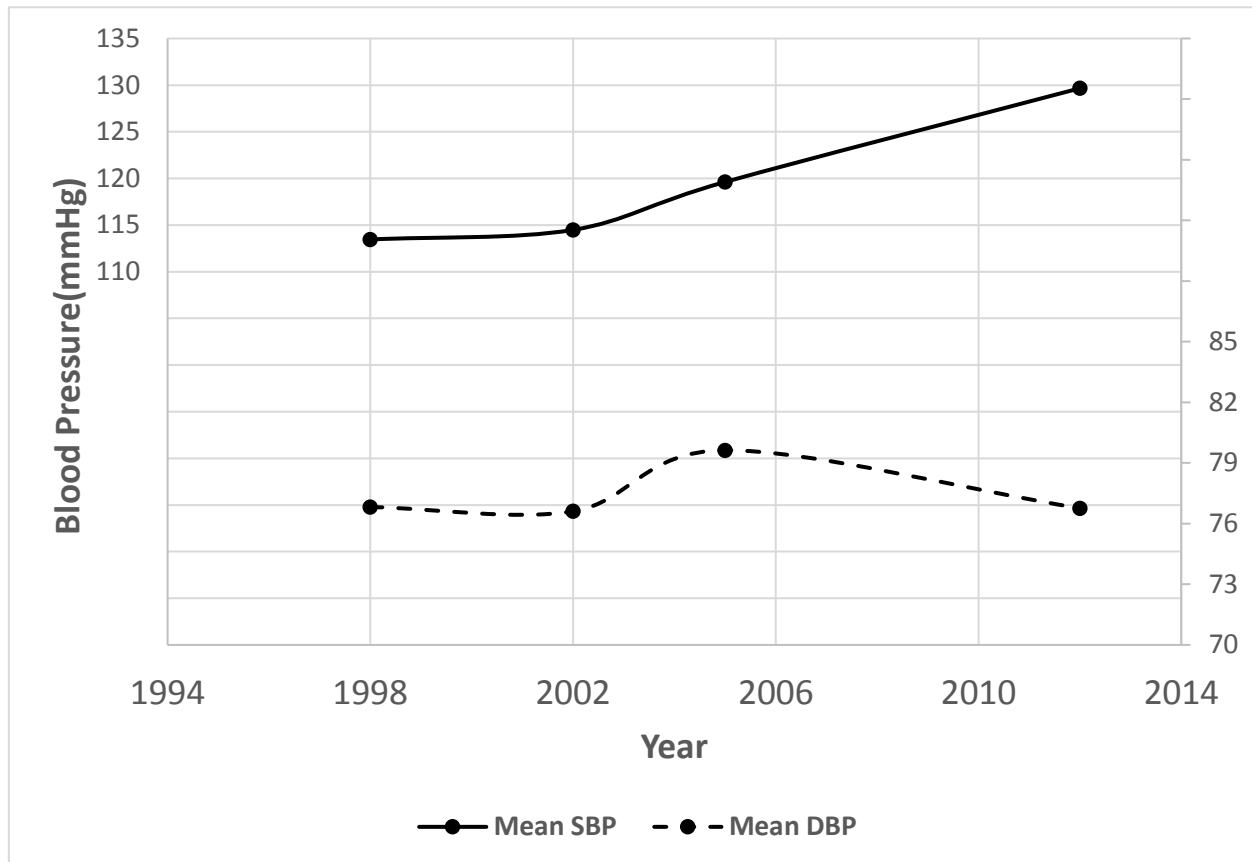
Overall, we observe increases in population mean SBP and DBP from 1998 through 2005 (**figure 2**). However, SBP and DBP diverge through the rest of follow-up, resulting in increases in PP between 2005 and 2012. Mean and changes in BP and PP differ according to baseline age. **Figure 3** shows BP trajectories, stratified by baseline age groups. A secular trend in SBP is apparent: Women who were 50 years old in 2012 had higher SBP and PP than women who were 50 years old in 1998 (fig. 3) indicating a secular trend of  $\sim 7$  and  $\sim 9$  mmHg, respectively. A similar secular trend was not observed for DBP. Women  $>55$  y in 1998 had the highest mean SBP and DBP in 2012 (143.87 and 80.33 mmHg, respectively). However, these and the second oldest age group had similarly high mean 2012 PP ( $>60$  mmHg). We observe similar secular trends in BP and PP when only participants who were present through all survey rounds are considered (**Supp. Figure 1**). The number of barangays increased since the CLHNS began in 1983, as women moved throughout Metro Cebu. Mean UI for the original 33 barangays rose over time. Non-movers lived in more urban barangays from 2002 onward (**figure 4**). Participants who moved before 2002 and 2005 had the lowest median UI in the population. Evidently, changes in UI over time occurred in multiple directions in spite of moving: without change, from less to more urban, and vice-versa. Our **figure 5** shows that movers tend to have higher UI increases than non-movers for most of follow-up. The largest contrast was observed in 2005, when movers had a median UI increase of 12 units compared to 3 in non-movers. Movers also had larger UI decreases compared to non-movers throughout follow-up. In spite of the direction of changes in UI, the same magnitude of change in UI from 2005 through 2012 was observed in both moving groups.

## Change in BP models

Results are presented as coefficients from a series of mixed effects longitudinal regression models of change in SBP, DBP, and PP. Based on the DAG analysis, and after backward elimination, final models considered survey year, previous UI, previous wealth score quintile, age, and moving as

covariates in our models. Interaction terms test heterogeneity of effects of change in UI on change in BP and PP across levels of previous UI; moving on changes in BP and PP across levels of previous UI, and change in UI on change in PP across age.

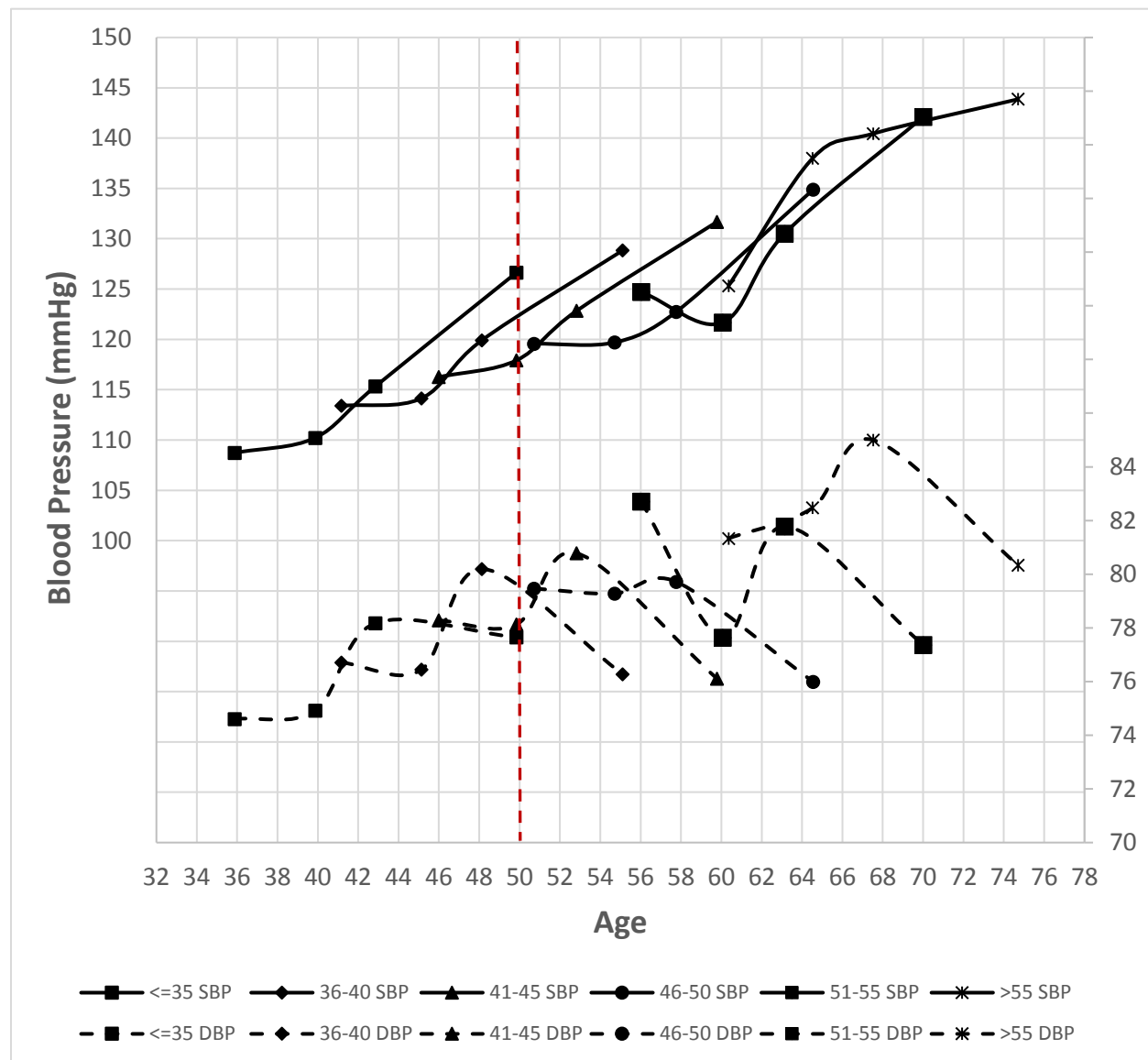
**Figure 2. Mean systolic and diastolic blood pressure\* of CLHNS women by survey year†**



\*Blood pressure (BP) was measured from 1998 in triplicate after a 10-minute seated rest using mercury sphygmomanometers. Means were derived from the average of three BP measurements. Solid lines represent SBP and dashed lines DBP. SBP and DBP values are shown on the left and right axis, respectively.

† 1998, 2002 2005, and 2012

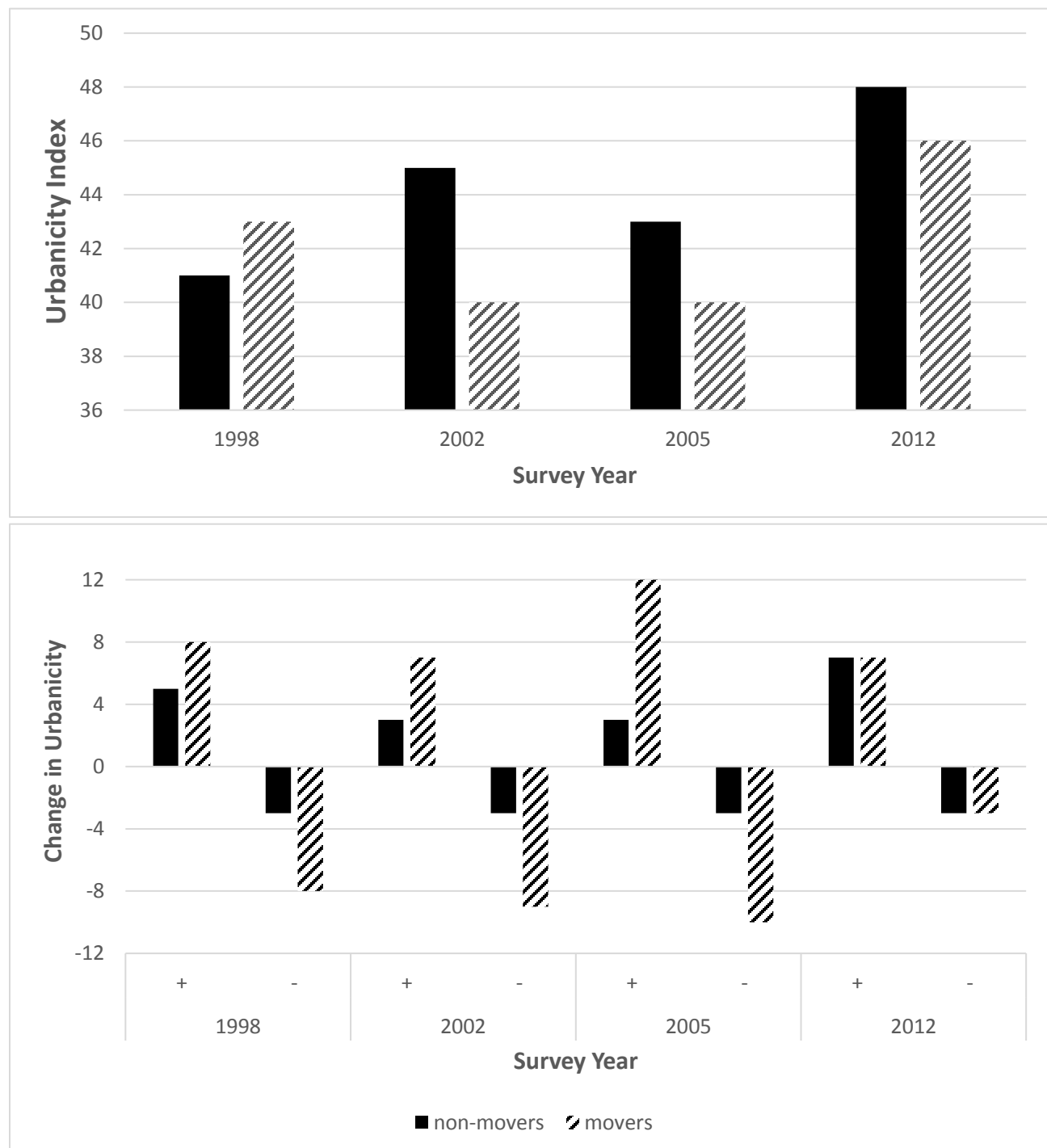
**Figure 3. Observed secular trends in SBP\* and DBP from 1998-2012 stratified by baseline age groups†**



\*Blood pressure (BP) was measured from 1998 in triplicate after a 10-minute seated rest using mercury sphygmomanometers. Means were derived from the average of three BP measurements. Solid lines represent SBP and dashed lines DBP. SBP and DBP values are shown on the left and right axis, respectively.

† Based on age when participants first participated from 1998-2012. Every data point represents blood pressure at the mean age within each age group.

**Figure 4. Observed median Urbanicity Index\* by survey year, moving patterns, and direction of urbanization†**



\*Multicomponent index that represents a gradient from rural to urban. It is derived from community surveys each survey year that reflects population size and density, community infrastructure, economic and environmental characteristics. Increasing continuous amount represent higher urban characteristics.

†Positive and negative changes in urbanicity are denoted by the + and - signs, respectively

**SBP:** The main effect of change in UI was positively and significantly associated with a 0.32 mmHg change in SBP (95%CI: 0.06, 0.57 P=0.015). The effects of change in UI and moving on change in SBP were significantly heterogeneous across levels of previous UI (95%CI: -0.02, -0.032E-1 and -0.19, 0.01 P<0.1). Survey year was significantly and positively associated with SBP increases >4 mmHg in 2005 and 2012 compared to 2002 (**Table 2**).

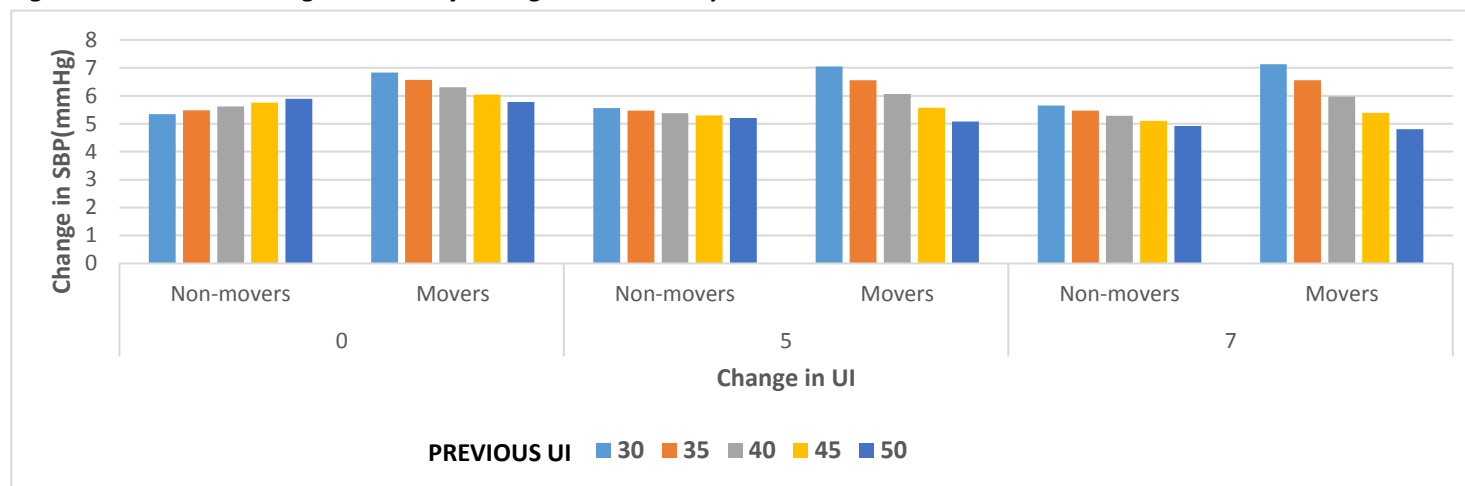
To aid in the understanding of SBP model results, we simulate specific conditions to predict the mean change in SBP through follow-up based on the estimated regression model below and offer and interpretation of results through a series of graphs. For example: (1) *Movers who experienced no change in UI and initially lived in barangays of UI levels of 30 have a predicted change in SBP of ~6.84 mmHg (figure 5)*. (2) *35 y old movers who experienced no change in UI and lived in barangays of UI levels of 41 have a predicted change in SBP of ~4.71 mmHg (figure 6)*. Conditions are denoted below:

$$\text{Predicted SBP} = \beta_0 + \beta_1 X_1 + \beta_2 X_{2, \text{year}} + \beta_3 X_3 + \beta_4 X_3 X_1 + \beta_5 X_4 + \beta_6 X_4 X_3 + \beta_7 X_{5, Q_i \text{wealth}} + \beta_8 X_6 + \beta_9 X_6^2 + \beta_{10} X_6^3 + \epsilon$$

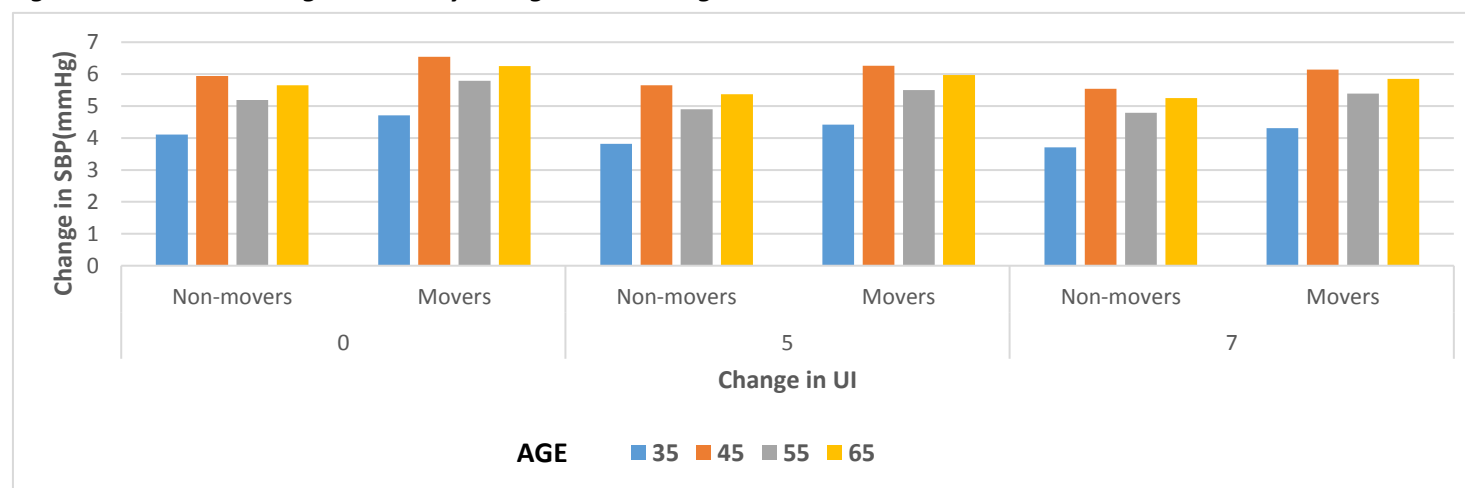
Where:

$X_1$ = Change in UI (0, 5, 7)	$\beta_4$ = Change in expected SBP by change in UI-previous UI interaction (increases in slope due to increments in previous UI)
$X_2$ = Survey Year (on average)	
$X_3$ = Previous UI (30, 35, 40, 45, 50)	
$X_3 X_1$ = Change in UI-Previous UI interaction	$\beta_5$ = Change in expected SBP by moving
$X_4$ = Moving (movers compared to non-movers)	$\beta_6$ = Change in expected SBP by moving-previous UI interaction (increases in previous UI slope due to moving)
$X_4 X_3$ = Moving-Previous UI interaction	$\beta_7$ = Change in expected SBP by quintile of wealth score compared to 1 <sup>st</sup> quintile.
$X_5$ = Previous wealth score quintile (held constant)	
$X_6^n$ = Age to the n power (50 y)	$\beta_8$ = Change in expected SBP per unit changes in age
$\epsilon$ =Error term	$\beta_9$ = Change in expected SBP per unit changes in squared age
$\beta_0$ = Constant value when $X_i = 0$	$\beta_{10}$ = Change in expected SBP per unit changes in age cubed
$\beta_1$ = Change in expected SBP by unit changes in UI	
$\beta_2$ = Change in expected SBP by survey year	
$\beta_3$ = Change in expected SBP by unit changes in previous UI	

**Figure 5. Predicted change in SBP\* by change in UI across previous UI†**



**Figure 6. Predicted change in SBP\* by change in UI and age†**



\*Blood pressure (BP) was measured from 1998 in triplicate after a 10-minute seated rest using mercury sphygmomanometers. Means were derived from the average of three BP measurements. Solid lines represent SBP and dashed lines DBP. SBP and DBP values are shown on the left and right axis, respectively.

†Multicomponent index that represents a gradient from rural to urban. It is derived from community surveys each survey year that reflects population size and density, community infrastructure, economic and environmental characteristics. Increasing continuous amount represent higher urban characteristics.

**DBP:** The effect of change in UI on change in DBP was heterogeneous according to previous levels of UI ( $p < 0.1$ ). The main effect of moving and its interaction with previous UI were significantly associated with change in DBP, but in opposite directions (**Table 2**). Cubic age had a significantly positive relationship with change in DBP ( $0.54E-3$  | 95%CI:  $8.25E-5$ ,  $0.10E-3$   $P < 0.05$ ). Survey year was significantly associated with a  $>3$  mmHg increase in 2005 and a decrease of just over 1 mmHg DBP in 2012, compared to 2002.

To aid in the understanding of DBP model results, we simulate specific conditions to predict the average change in DBP through follow-up based on the estimated regression model below and offer an interpretation of results through a series of graphs. For example, (1) *Movers who experienced no change in UI and lived at a UI level of 30 have an expected change in DBP of  $\sim 1.73$  mmHg (figure 7)*. (2) *35 y old movers who experienced no change in UI and lived in barangays of UI levels of 41 have an expected decrease in DBP of  $\sim 0.32$  mmHg (figure 8)*. Conditions are denoted below:

$$\text{Predicted DBP} = \beta_0 + \beta_1 X_1 + \beta_2 X_{2, \text{year}} + \beta_3 X_3 + \beta_4 X_3 X_1 + \beta_5 X_4 + \beta_6 X_4 X_3 + \beta_7 X_{5, Q_1 \text{wealth}} + \beta_8 X_6 + \beta_9 X_6^2 + \beta_{10} X_6^3 + \epsilon$$

Where:

$X_1$  = Change in UI (0, 5, 7)

$X_2$  = Survey Year (on average)

$X_3$  = Previous UI (30, 35, 40, 45, 50)

$X_3 X_1$  = Change in UI-Previous UI interaction

$X_4$  = Moving (movers compared to non-movers)

$X_4 X_3$  = Moving-Previous UI interaction

$X_5$  = Previous wealth score quintile (held constant)

$X_6^n$  = Age to the  $n$  power (50 y)

$\epsilon$  = Error term

$\beta_0$  = Constant value when  $X_i = 0$

$\beta_1$  = Change in expected DBP per unit changes in UI

$\beta_2$  = Change in expected DBP by survey year

$\beta_3$  = Change in expected DBP per unit changes in previous UI

$\beta_4$  = Change in expected DBP by change in UI-previous UI interaction (increases in slope due to increments in previous UI)

$\beta_5$  = Change in expected DBP by moving

$\beta_6$  = Change in expected DBP by moving-previous UI interaction (increases in previous UI slope due to moving)

$\beta_7$  = Change in expected DBP by quintile of wealth score compared to 1<sup>st</sup> quintile.

$\beta_8$  = Change in expected DBP per unit changes in age

$\beta_9$  = Change in expected DBP per unit changes in squared age

$\beta_{10}$  = Change in expected DBP per unit changes in age cubed



Figure 7. Predicted change in DBP\* by change in UI across previous UI†

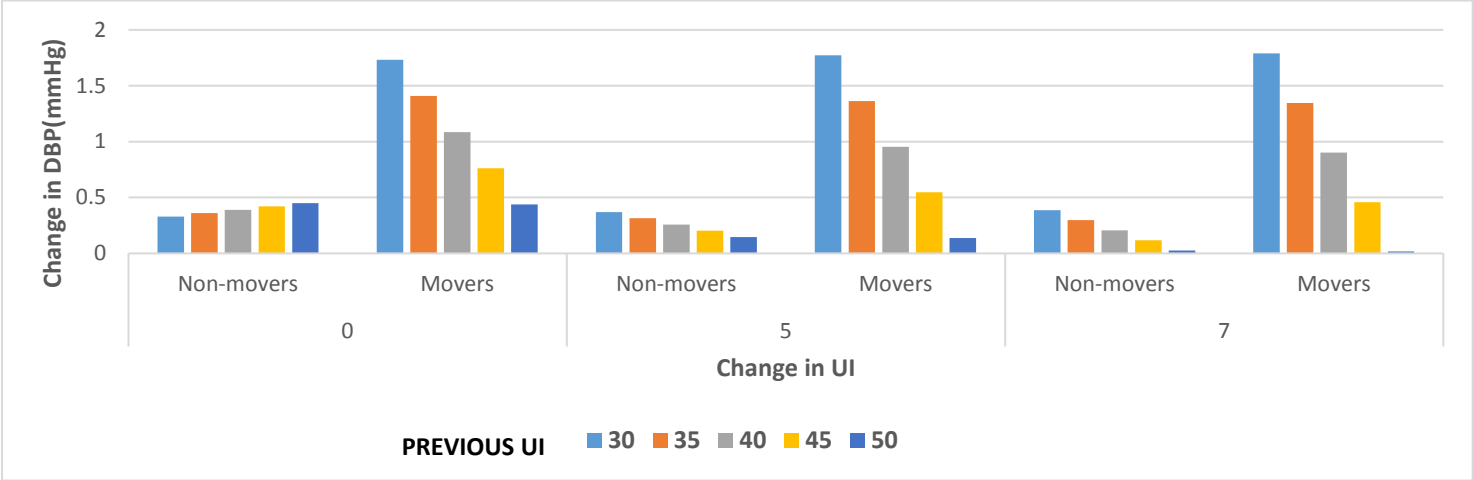
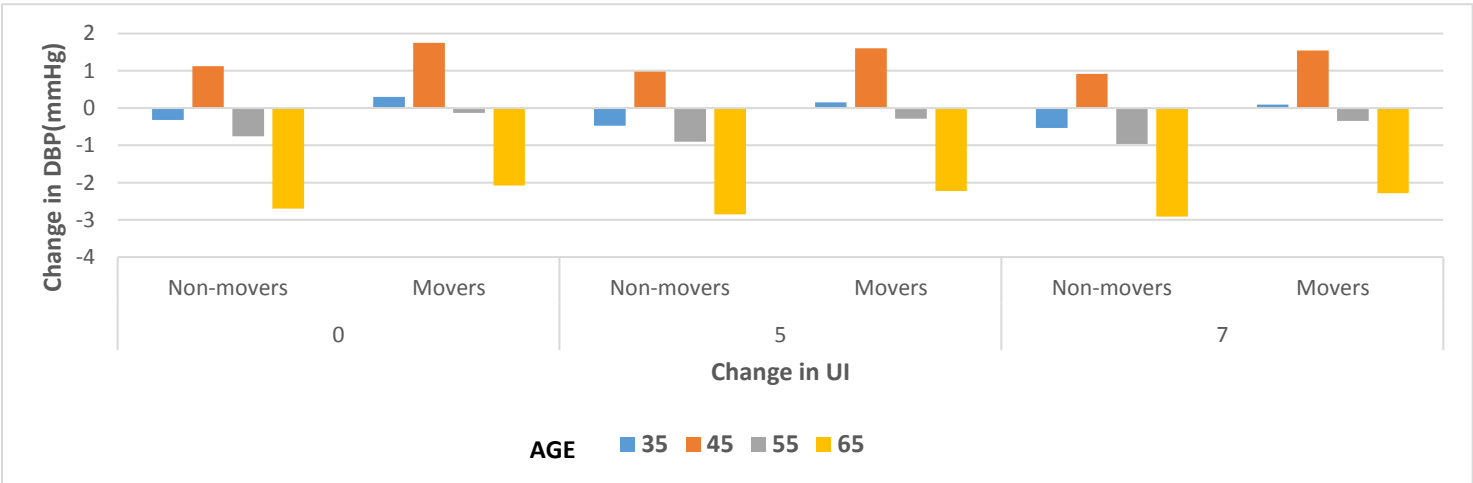


Figure 8. Predicted change in DBP\* by change in UI across age†



\*Blood pressure (BP) was measured from 1998 in triplicate after a 10-minute seated rest using mercury sphygmomanometers. Means were derived from the average of three BP measurements. Solid lines represent SBP and dashed lines DBP. SBP and DBP values are shown on the left and right axis, respectively.

†Multicomponent index that represents a gradient from rural to urban. It is derived from community surveys each survey year that reflects population size and density, community infrastructure, economic and environmental characteristics. Increasing continuous amount represent higher urban characteristics.

**PP:** The effect of change in UI on change in PP was significantly heterogeneous across levels of previous UI and cubic age ( $p<.001$ ). Neither the main effect of moving nor its interaction with previous UI are significantly associated with change in PP (**Table 2**). Survey year is positively associated with PP increases in both 2005 and 2012 compared to 2002. However, this association is significant only in 2012 (10.56 mmHg | 95%CI: 9.44, 11.67,  $p<0.01$ ).

To aid in the understanding of PP model results, we simulate specific conditions to predict change in PP based on the estimated regression model below and offer interpretation of graphed results. For example, (1) *Movers who experienced no change in UI and lived in barangays with UI levels of 30 have an expected change in PP of ~5.03 mmHg (figure 9)*. (2) *35 y old movers who experienced no change in UI and lived in barangays of UI levels of 41 have an expected increase in PP of ~3.84 mmHg (figure 10)*. Conditions are denoted below.

$$\text{Predicted PP} = \beta_0 + \beta_1 X_1 + \beta_2 X_{2,year} + \beta_3 X_3 + \beta_4 X_3 X_1 + \beta_5 X_4 + \beta_6 X_4 X_3 + \beta_7 X_{5,Q_i wealth} + \beta_8 X_6 + \beta_9 X_6 X_1 + \beta_{10} X_6^2 + \beta_{11} X_6^2 X_1 + \beta_{12} X_6^3 + \beta_{13} X_6^3 X_1 + \epsilon$$

Where:

$X_1$  = Change in UI (0, 5, 7)

$X_2$  = Survey Year (2005 and 2012 compared to 2002)

$X_3$  = Lagged UI (30, 35, 40, 45, 50)

$X_3 X_1$  = Change in UI-Previous UI interaction

$X_4$  = Moving (movers compared to non-movers)

$X_4 X_3$  = Moving-Previous UI interaction

$X_5$  = Lagged wealth score quintile (held constant)

$X_6^n$  = Age to the n power (50 y)

$\epsilon$  = Error term

$\beta_0$  = Constant value when  $X_i = 0$

$\beta_1$  = Change in expected PP per unit changes in UI

$\beta_2$  = Change in expected PP by survey year compared to 2002

$\beta_3$  = Change in expected PP per unit changes in previous UI

$\beta_4$  = Change in expected PP by change in UI-previous UI interaction (increases in slope due to increments in previous UI)

$\beta_5$  = Change in expected PP by moving

$\beta_6$  = Change in expected PP by moving-previous UI interaction (increases in previous UI slope due to moving)

$\beta_7$  = Change in expected PP by quintile of wealth score compared to 1<sup>st</sup> quintile.

$\beta_8$  = Change in expected PP per unit changes in age

$\beta_9$  = Change in expected PP by age-change in UI interaction (changes in age slope due to changes in UI)

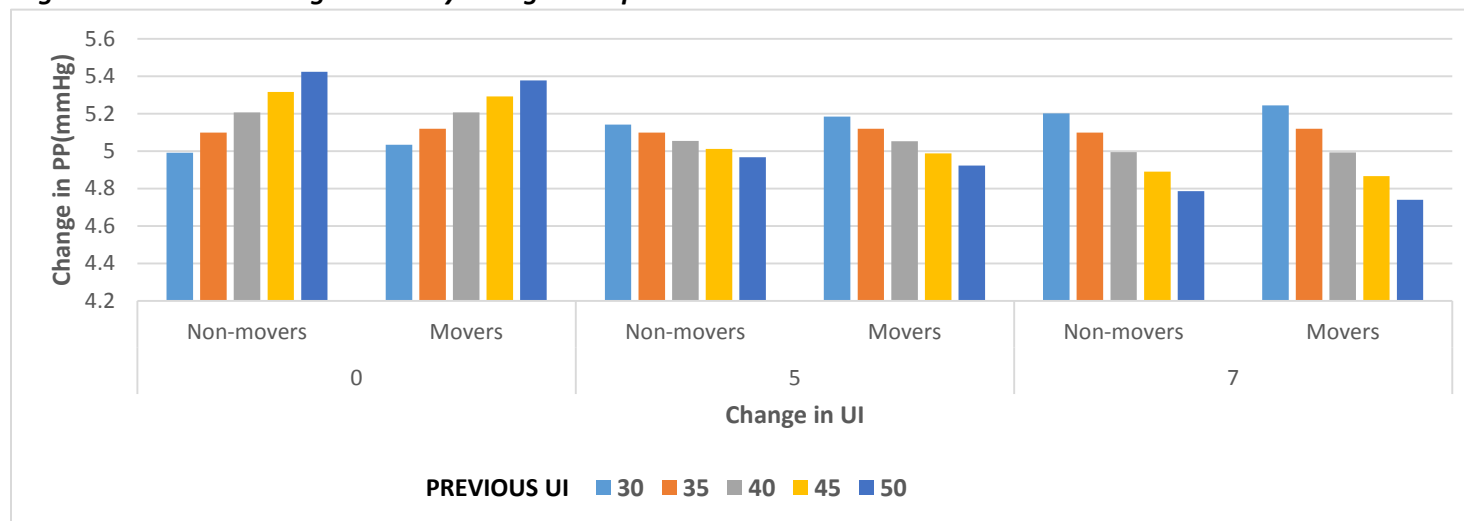
$\beta_{10}$  = Change in expected PP per unit changes in squared age

$\beta_{11}$  = Change in expected PP by squared age-change in UI interaction (changes in squared age slope due to changes in UI)

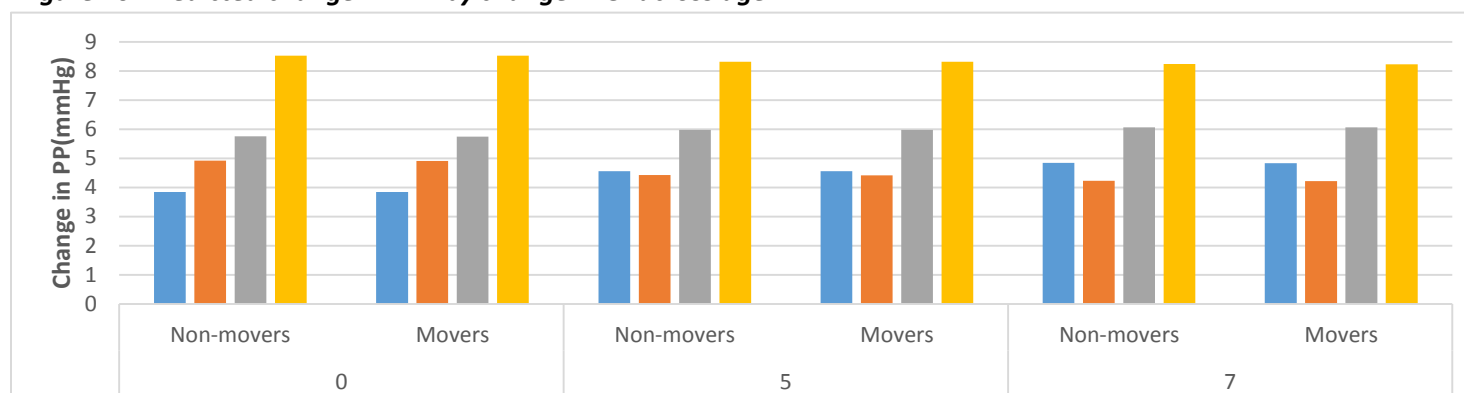
$\beta_{12}$  = Change in expected PP per unit changes in cubic age

$\beta_{13}$  = Change in expected PP by cubic age-change in UI interaction (changes in cubic age slope due to changes in UI)

**Figure 9. Predicted change in PP\* by change in UI previous UI†**



**Figure 10. Predicted change in PP\* by change in UI across age†**



\*Blood pressure (BP) was measured from 1998 in triplicate after a 10-minute seated rest using mercury sphygmomanometers. Means were derived from the average of three BP measurements. Solid lines represent SBP and dashed lines DBP. SBP and DBP values are shown on the left and right axis, respectively.

†Multicomponent index that represents a gradient from rural to urban. It is derived from community surveys each survey year that reflects population size and density, community infrastructure, economic and environmental characteristics. Increasing continuous amount represent higher urban characteristics.

**TABLE 2. Final Change in BP by change in UI model results output.**

		Change in BP models		
		SBP $\beta$ (SE)	DBP $\beta$ (SE)	PP $\beta$ (SE)
<b>N (# observations:participants)</b>		5614:2107	5614:2107	5614:2107
<b>Change in Urbanicity</b>		0.32(0.06,0.57)*	0.11(-0.06,0.28)	13.13(-0.06,26.33)
<b>Previous Urbanicity</b>		0.03(-0.01,0.07)	0.01(-0.02,0.03)	0.02(-0.01,0.05)
<b>Survey Year</b>				
	<b>2002</b>	<b>1(ref)</b>	<b>1(ref)</b>	<b>1(ref)</b>
	<b>2005</b>	4.15(2.97,5.32)*	3.58(2.79,4.36)*	0.5(-0.39,1.4)
	<b>2012</b>	9.61(8.16,11.07)*	-1.06(-2.03,-0.09)*	10.56(9.44,11.67)*
<b>Change in Urbanicity*Previous Urbanicity interaction</b>		-0.01(-0.01,0)*	0(-0.01,0)*	-0.01(-0.01,0)*
<b>Migration Pattern</b>				
	<b>Non-movers</b>	<b>1(ref)</b>	<b>1(ref)</b>	<b>1(ref)</b>
	<b>Movers</b>	3.9(0.04,7.76)*	3.52(0.93,6.1)*	0.17(-2.75,3.1)
<b>Migration Pattern*Previous Urbanicity Interaction</b>		-0.08(-0.17,0.01)*	-0.07(-0.13,-0.01)*	0(-0.07,0.06)
<b>Lagged Wealth Asset Score Quintile</b>				
	<b>2</b>	0.06(-1.41,1.52)	-0.18(-1.16,0.81)	0.24(-0.87,1.35)
	<b>3</b>	0.54(-0.97,2.05)	-0.37(-1.38,0.64)	0.95(-0.2,2.09)
	<b>4</b>	0.22(-1.31,1.75)	-0.37(-1.4,0.65)	0.6(-0.56,1.76)
	<b>5</b>	-0.24(-1.78,1.31)	-0.68(-1.71,0.36)	0.44(-0.73,1.61)
<b>Age</b>		5.02(-0.59,10.62)	4.74(0.98,8.5)*	2.37(-2.32,7.06)
<b>Change in Urbanicity*Age interaction</b>		--	--	-0.79(-1.56,-0.01)*
<b>Age squared</b>		-0.1(-0.21,0.01)	-0.09(-0.16,-0.02)*	-0.05(-0.14,0.04)
<b>Change in Urbanicity*Age squared interaction</b>		--	--	0.02(0,0.03)*
<b>Age cubed</b>		0(0,0)	0(0,0)*	0(0,0)
<b>Change in Urbanicity*Age cubed interaction</b>		--	--	0(0,0)*

\*Denotes statistical significance at  $\alpha < 0.05$  for main effects and  $< 0.1$  for interaction terms.

### Change in BP by Change in UI

We simulated changes in BP and PP in 2005 and 2012 by changes in UI in participants with the same age (50 y) who previously resided in different UI levels (30, 35, 40, 45, and 50), and in participants living in the same UI level (UI= 41) at different ages (35, 45, 55, and 65 y). Our simulations predicted that among non-movers, those who previously lived in the most urban barangays had the highest predicted change in SBP, DBP, and PP compared to less urban dwellers when they experienced no change in UI. However, as UI increases, BP and PP changes seem to shift towards those residing in less urban

barangays. This shift is apparent in movers for PP. However, movers who previously lived in the least urban barangays were found to consistently have higher predicted BP compared to their more urban counterparts across levels of UI (**figs 5, 7, and 9**). In spite of moving and changes in UI, we predicted higher increases in SBP in 45 and 65 y olds compared to 35 and 55 y olds (**fig 6**). The highest increases and decreases in predicted DBP were also found in the former group (**fig 8**). Predicted PP was consistently highest among older versus younger participants (**fig 10**). However, predicted change in PP for 35 y olds becomes higher than 45 y olds' as UI increases.

### Medication model

Compared to 2002, participants with hypertension in 2005 were 1.35 times (non-significantly) more likely to use medication (OR= 1.35 | 95%CI: 0.98, 1.88) while participants in 2012 were ~64% less likely to use medication (OR= 0.36 | 95%CI: 0.23, 0.56 P<0.01). The association of medication use with change in urbanicity is positive, but non-linear, leveling off at higher change in urbanicity as indicated by the significant squared term. Moving was non-significantly associated with a 17% decreased likelihood of using medication. Being in the second wealth score quintile is non-significantly associated with a 53% increase likelihood of using medication compared to the lowest quintile. However, those in the third, fourth, and fifth are >2.5 times as likely to use anti-hypertensive medication (**Table 3**).

<b>TABLE 3. Full medication model results.</b>		
N (# obs)		2137:1201
		Odds Ratio (95%CI)
Survey Year	2005	1.35(0.98,1.88)
	2012	0.36(0.23,0.56)*
Change in Urbanicity		0.99(0.97,1.01)
Squared Change in Urbanicity		1(1,1)*
Age		1.02(0.99,1.05)
Migration Pattern	Migrated	0.83(0.52,1.31)
Lagged Wealth Asset Score Quintile	2	1.53(0.87,2.69)
	3	2.51(1.46,4.33)*
	4	2.83(1.65,4.86)*
	5	3.24(1.89,5.55)*

\*Denotes statistical significance at  $\alpha < 0.05$

## Mortality outcome models

**SBP:** Every 1 mm Hg increase in SBP in 2005 is significantly associated with a 4% increased likelihood of hypertension-related mortality between 2005 and 2012 (95% CI: 1.02, 1.05 P<0.001). Every unit increase in age in 2005 is non-significantly associated with a 5% increased likelihood of hypertension-related mortality between 2005 and 2012 (95%CI: 0.99, 1.11 P=0.094).

**DBP:** Every 1 mm Hg increase in DBP in 2005 is significantly associated with a 7% increased likelihood of hypertension-related mortality between 2005 and 2012 (95%CI: 1.05, 1.09 P<0.001). Every unit increase in age in 2005 is significantly associated with a 7% increased likelihood of hypertension-related mortality in 2012 (95%CI: 1.01, 1.13 P=0.015).

**PP:** Every 1 mm Hg increase in PP in 2005 is significantly associated with a 4% increased likelihood of hypertension-related mortality between 2005 and 2012 (95%CI: 1.02, 1.06 P<0.001). Every unit increase in age in 2005 is non-significantly associated with a 5% increased likelihood of hypertension-related mortality between 2005 and 2012 (95%CI: 0.99, 1.11 P=0.076).

Full mortality outcome model results output are displayed in **table 4** below.

TABLE 4. Mortality outcome model results *			
	Outcome Models		
	SBP β (95%CI)	DBP β (95%CI)	PP β (95%CI)
N (# obs)	2001	2001	2001
Mean SBP	1.04(1.02,1.05)†	--	--
Mean DBP	--	1.07(1.05,1.09)†	--
Mean PP	--	--	1.04(1.02,1.06)†
Age	1.05(0.99,1.11)	1.07(1.01,1.13)†	1.05(0.99,1.11)

\*Models were adjusted for 2005 SBP, DBP, and PP, separately; and 2005 age. 36 total hypertension-related deaths were found in our final analytic sample.

† Denotes statistical significance at  $\alpha < 0.05$  for main effects

## CHAPTER 2: DISCUSSION AND SYNTHESIS

### Discussion and Synthesis

#### Overview of major findings

From 1998 through 2012, we observed that SBP consistently increased and DBP peaked in 2005. As anticipated, we observed the greatest population-level increases in PP between 2005 and 2012. In 1998, the median SBP, DBP, and PP were 110, 78.67, and 40 mmHg, respectively. Their 2012 median values were 124.33, 75.67, and 49.33 mmHg, respectively. Trends in BP highlight important secular and age-related changes in blood and pulse pressures. We observed that younger participants had higher SBP, lower DBP, and higher PP in 2012 compared to individuals of the same age in 1998. Restriction of this analysis to those women with complete data suggest that this is a true secular trend, not explained by the higher mortality and thus lower representation of older women in the 2012 sample.

Modernization and urban development were responsible for UI increases in the original 33 CLHNS barangays. At an individual level, UI increases among movers reflected the tendency for these to move from less to more urban barangays. Individual decreases in UI do not necessarily indicate reversion of the urbanization process. Among movers, declines in UI reflect moving to less urbanized barangays in Metro Cebu. In addition, several newly imposed barangay political boundaries affected how urban characteristics distributed over time in Metro Cebu. Overall, most of the sample tended to experience positive changes in UI.

Different communities may have the same UI score according to their individual components that drive urbanicity (i.e. population density, access to hospitals, etc.). Thus, participants may have moved between communities with different characteristics but the same UI score.

Our observed age-related BP changes align with the notion that SBP and DBP increase in early adulthood. The continued SBP increase and DBP decrease from middle adulthood through later in life associated with age-related arterial stiffness and peripheral vascular resistance<sup>18,19</sup>, respectively, thus led to higher PP with age.

#### Comparison with previous literature

BP trajectories with age in our cohort align with other longitudinal cohorts. For example, in a longitudinal cohort of close to 5,000 participants from the Framingham Offspring Study<sup>20</sup> with multiple BP measurements who were followed through 6 survey rounds in the 1971-1998 period, SBP and DBP rose through middle adulthood, when DBP declined as SBP kept rising after. SBP trends differed by gender in this cohort, with steeper increases seen in women compared to men. A sample of women aged 38-60 y from Gothenburg, Sweden experienced similar changes in SBP and DBP in a 24 y-period.<sup>21</sup> However, SBP declined after ~80 y in this cohort at a faster rate than DBP, thus resulting in PP declines. Secular BP patterns in our study differ from those found in the Tromsø study in northern Norway which found greater declines in mean SBP and DBP from 1979 through 2008 among women participants compared to men.<sup>22</sup> Interestingly, SBP increased with age at a faster rate for older cohorts born 1920-1949 compared to their younger counterparts born 1950-1977. While men experienced DBP peaks when these were 50-60 y of age, women reached peaks in DBP at different biological ages. However, this study was limited in that 41% of its analytic sample had 1 measurement through 5 survey rounds. No cohort differences in SBP or its changes were found among participants of the Fels Longitudinal Study aged 18-40 y and born 1920-1979.<sup>23</sup> However, secular DBP patterns show that the youngest participants start adulthood with lower DBP than their older counterparts (at the same age), but continue through



middle-adulthood with higher DBP. Furthermore, mean rates of DBP increase are ~3 times faster in the youngest versus oldest cohort, even after adjusting for BMI. While many large cross-sectional epidemiological studies document secular decreases in SBP and DBP over time, these fail to account for individual change in BP.<sup>24-26</sup> Recent work from the China Health and Nutrition Survey (CHNS) highlights secular and temporal changes in blood pressure through an 18-year period.<sup>27</sup> The oldest CHNS women (born in 1940) experienced greater increases in SBP and DBP from 1991 through 2009 compared to their younger counterparts (born in 1970s) across levels of UI. However, the difference in DBP increases between these age cohorts was larger at lower UI.

The current literature investigating the urbanicity-BP relationship is mostly comprised of cross-sectional studies, with few exceptions from prospective longitudinal cohort studies.<sup>20-23, 27</sup> Studies incorporating migration into the mix are less prevalent. Despite the inability to infer how temporal changes in urbanicity relate to BP and PP from cross-sectional studies, we can't ignore important previous insights that help explain the complex nature of urban health. In previous work in the contexts of India and Cameroon<sup>28, 29</sup>, exposure to urbanicity has previously been quantified based on retrospective recall of lifetime duration of residence. While no appreciable differences were found in SBP or DBP across genders with respect to exposure to urban life-years in an Indian cohort, every 10 year increase in this parameter was positively associated with both SBP and DBP. Meanwhile, recent Cameroonian urban dwellers (<=2 years of exposure to an urban environment) were observed to have higher SBP than rural dwellers under the same exposure category. Exposure to urbanicity by migration has been addressed by comparing urban dwellers and their rural sibling counterparts.<sup>30</sup> In India, urban and migrant women were found to have >20% increased odds of hypertension, compared to rural women. In both men and women CHNS participants who resided below the 25<sup>th</sup> percentile of urbanicity, younger cohorts consistently had higher SBP and DBP than older cohorts (at the same biological age). In addition, younger cohorts had larger and smaller temporal increases in DBP and SBP, respectively. SBP

and DBP were similarly comparable across cohorts residing in the 75<sup>th</sup> percentile of urbanicity. However, cohort differences in DBP in women were statistically significant only in the context of low urbanicity.

### Limitations and Strengths

The present study has various limitations worth mentioning. Undoubtedly, our observed and estimated changes in BP may be affected by the level of medication awareness and actual medication use in participants. While interviewees were asked specifically about use of medications to treat hypertension, some participants may have misreported on their medication use with respect to its purpose. Similarly, participant mortality causes were reported by available household members and not medical records. However, a comparison of reported versus death certificate-listed cause of death in a subset of participants indicated a high level of concordance. Another weakness is that by design, our study population is contained within the Metro Cebu area. Therefore, it is currently impossible to assess how migration affects BP among participants who out-migrated to the capital (Manila) or other cities or countries, thus limiting the generalizability of our findings. Effectively, 78% of attrition in the CLHNS is attributed to out-migration from the Metro Cebu area.<sup>31</sup> We also only considered participants who moved between survey years as migrants with no consideration of migration frequency within survey intervals, which ranges from 4 to 7 years. We expect that frequent migrants may differ from less frequent counterparts with respect to exposure to UI through their lives.

Our study also has multiple strengths. To our knowledge, this is the first study to assess the longitudinal relationship between changes in UI and changes in SBP, DBP, and PP separately in a cohort of Filipino women. In addition, our study is the first to quantify longitudinal changes in UI due to migration CLHNS mothers. By including wealth, survey year, and non-linear age terms, our statistical models help shed light on previously unexplored complex relationships between level of UI, its change, migration, and secular and temporal changes in BP. With our ability to analyze individual changes in UI, BP, and other covariates in stayers and migrants, we ensure temporality in our analyzed relationships, a

crucial element of causal inference. Another strength is the use of our multi-component UI. The use of continuous UIs has been previously shown to better represent environmental heterogeneity within regions compared to dichotomous urbanicity variables (urban/rural) typically used in a variety of international settings.<sup>16, 32-37</sup>

### Public Health Implications and Conclusions

Our findings have important public health implications given the independent associations of PP with stroke, myocardial infarction, and other CVD outcomes.<sup>6,19,21,38</sup> This is further reinforced by the observed secular and temporal BP and PP changes in the youngest and oldest CLHNS participants. Our study echoes previous work in the CHNS highlighting the importance of BP screening in rural areas.<sup>27</sup> Our work adds attention to the young and migrant CLHNS populations. Efficient blood pressure surveillance systems are vital for the proper monitoring of BP and PP trajectories in the adult population. Age-specific efforts may be required to raise awareness among Filipino individuals at different stages of adulthood about the importance of tracking blood pressure, maintenance of healthy blood pressure, and how proximal factors influenced by the environment (e.g. air and noise pollution, highly processed foods, crime, stress) affect it. BP monitoring and surveillance may help shed light on the prevalence and incidence of untreated hypertension across ages in rural areas with poor access to hospitals. This is crucial given that hypertension is considered as one of the most important modifiable risk factors for CVD events.

To understand how urban life affects BP, it is crucial to consider the magnitude of change in UI, when (in age) this change occurs, and the levels of UI from where these changes are occur over time (be it by staying or migrating). We found that migrants who previously lived in the most rural barangays have the highest predicted increases in SBP and DBP, and PP as their exposure to UI increases. In addition, we found that at the same level of previous UI, the oldest individuals have the highest predicted PP values in spite of moving and being exposed to changes in UI. However, we also found that

as UI increases, so does the predicted PP in 35 y olds, eventually reaching levels comparable to 45 y olds. Future research in the CLHNS context may elucidate BP trajectories through the latter stages of the life course in adult Filipino women. New insights are vital to understanding the relationship between the environment and blood pressure in the current and future generations of Filipino mothers.

## APPENDIX 1: ADDITIONAL RESULTS

**Supplemental Table 1. Correlation matrix of household asset variables\* included in household wealth score.**

	Own a tv	Own a fridge	Own a bicycle	Own a vehicle	Own a china	Number of rooms in house	Toilet Quality	Housing Quality	Source of Water	Access to electricity	Cooking Fuel
Own a tv	1										
Own a fridge	0.42	1									
Own a bicycle	0.19	0.2	1								
Own a vehicle	0.19	0.3	0.11	1							
Own a china	0.18	0.27	0.09	0.17	1						
Number of rooms in house	0.33	0.31	0.14	0.21	0.14	1					
Toilet Quality	0.37	0.32	0.12	0.06	0.13	0.12	1				
Housing Quality	0.39	0.47	0.19	0.3	0.26	0.37	0.3	1			
Source of Water	0.25	0.21	0.1	0.08	0.12	0	0.4	0.2	1		
Access to electricity	-0.53	-0.3	-0.17	-0.1	-0.12	-0.24	-0.47	-0.36	-0.35	1	
Cooking Fuel	0.29	0.15	0.11	0.04	0.06	0.01	0.37	0.17	0.3	-0.36	1

\* The list of assets were based on the International Wealth Index (IWI). We modified the list of assets from the IWI based on available household-level characteristics assessed during the 1994 CLHNS household survey round by key informants and trained interviewers.

**SUPPLEMENTAL TABLE 1.1. NOTATION KEY FOR SUPPLEMENTARY TABLES 2-5**

<b>*</b>	All data derived from the Cebu Longitudinal Health and Nutrition Survey (CLHNS) 1998, 2002, and 2005, and 2012 survey rounds. Our analytic sample includes 2107 participants aged 29-62 y in 1998 with complete blood pressure and select demographic data. Continuous and categorical variables are expressed as “mean $\pm$ S.E” and “count (percent)”, respectively.
<b>†</b>	Total number of participants interviewed in each survey round.
<b>‡</b>	Based on self-reported age as of last birthday.
<b>§</b>	Multicomponent index that represents a gradient from rural to urban. It is derived from community surveys each survey year that reflects population size and density, community infrastructure, economic and environmental characteristics. Increasing continuous amount represent higher urban characteristics.
<b>#</b>	Participant’s change in UI score since the previous survey. 1998 values denote changes in UI since the 1994 CLHNS survey round.
<b>**</b>	Blood pressure (BP) was measured from 1998 in triplicate after a 10-minute seated rest using mercury sphygmomanometers.
<b>††</b>	See **
<b>‡‡</b>	Calculated from the difference between Systolic and Diastolic Blood pressures.
<b>§§</b>	Measured by trained specialists.
<b>##</b>	Height (m) and weight (kg) were measured at home by trained specialists using standardized methods.
<b>***</b>	Estimated energy intake (kcal) in one 24-hr recall per survey round. We use conversion factors to account for moisture and fat retention due to cooking methods (e.g. boiling, braising, and frying).
<b>†††</b>	Estimated weekly household income. Log transformation was performed due to income disparities in the Philippines.
<b>‡‡‡</b>	Based on participant’s self-reported highest attained education level. Participants who did not know or reported “N/A” were considered to not have completed a single grade.
<b>§§§</b>	Based on whether participants moved to different barangays between survey rounds.
<b>###</b>	Based on whether participants experienced null, positive, or negative changes in UI.

**SUPPLEMENTAL TABLE 2. Characteristics of a Longitudinal Cohort of Eligible Adult Filipino Women Participants from 1998-2012\***

Survey Year	1998		2002		2005		2012	
n†	1938		2072		2008		1818	
	Mean (S.E.)	Median	Mean (S.E.)	Median	Mean (S.E.)	Median	Mean (S.E.)	Median
Age‡	41.92(0.14)	41.22	45.87(0.13)	45.17	48.77(0.13)	48.03	55.56(0.14)	54.78
Urbanicity Index§	38.95(0.31)	41	41.3(0.31)	45	40.49(0.3)	43	43.96(0.3)	47
Systolic Blood Pressure**	113.45(0.41)	110	114.48(0.42)	110.67	119.62(0.45)	119.33	129.66(0.57)	124.33
Diastolic Blood Pressure††	76.82(0.27)	78.67	76.61(0.28)	75.33	79.63(0.28)	80	76.76(0.3)	75.67
Pulse Pressure‡‡	36.63(0.23)	40	37.87(0.25)	37.33	39.99(0.28)	40	52.9(0.37)	49.33
Waist Circumference§§	76.04(0.21)	75.2	78.59(0.22)	78	80.93(0.26)	80.6	82.05(0.27)	81.62
Body Mass Index##	23.65(0.09)	23.29	24.34(0.09)	24.19	24.35(0.1)	24.17	24.85(0.11)	24.71
Energy Intake***	1268.58(12.92)	1170.63	1208.02(13.21)	1106.59	1226.73(13.7)	1112.24	1082.86(13.92)	961
Log Income per Capita+++	0.96(0.01)	0.89	0.96(0.01)	0.89	0.95(0.01)	0.89	1.36(0.01)	1.27
	N	%	N	%	N	%	N	%
<b>Education Level †††</b>								
<6th Grade	1,094	56.45	1,212	58.49	1,172	58.37	1,071	58.91
7th-12th Grade	560	28.9	587	28.33	574	28.59	514	28.27
>High School Education	284	14.65	273	13.18	262	13.05	233	12.82
<b>Migration Status§§§</b>								
Stayed	1,770	91.33	1,943	93.77	1,930	96.12	1,107	60.89
Moved	168	8.67	129	6.23	78	3.88	702	38.61
missing	--		--		--		9	0.5
<b>Direction of Urbanization###</b>								
No change	132	6.81	177	8.54	390	19.42	123	6.77
Positive	1,399	72.19	1,511	72.92	608	30.28	1,281	70.46
Negative	288	14.86	372	17.95	1,009	50.25	414	22.77
missing	119	6.14	12	0.58	1	0.05	--	

**SUPPLEMENTAL TABLE 3. Characteristics of a Longitudinal Cohort of Eligible Adult Filipino Women Participants by Moving Status 1998-2012\***

Survey year	1998		2002		2005		2012	
n†	1938		2072		2008		1818	
	Stayed	Moved	Stayed	Moved	Stayed	Moved	Stayed	Moved
<b>Age‡</b>	42.04 (0.14)	40.65 (0.42)	45.97 (0.14)	44.34 (0.5)	48.84 (0.14)	47.17 (0.63)	55.83 (0.18)	55.09 (0.22)
<b>Urbanicity Index§</b>	38.82 (0.33)	40.29 (0.88)	41.35 (0.32)	40.49 (1.17)	40.55 (0.31)	38.97 (1.34)	45.29 (0.35)	41.93 (0.52)
<b>Change in Urbanicity#</b>	3.5 (0.09)	0.67 (1.02)	3.02 (0.1)	0.68 (1.22)	-0.63 (0.1)	-4.31 (1.59)	3.74 (0.13)	3.25 (0.31)
<b>Systolic Blood Pressure**</b>	113.37 (0.43)	114.33 (1.42)	114.45 (0.44)	114.93 (1.68)	119.6 (0.46)	120.28 (2.08)	129.76 (0.74)	129.41 (0.91)
<b>Diastolic Blood Pressure††</b>	76.8 (0.28)	77.02 (1)	76.59 (0.28)	76.95 (1.13)	79.59 (0.28)	80.57 (1.15)	76.76 (0.38)	76.77 (0.47)
<b>Pulse Pressure‡‡</b>	36.57 (0.24)	37.31 (0.76)	37.87 (0.26)	37.98 (0.84)	40 (0.29)	39.71 (1.38)	53 (0.47)	52.64 (0.58)
<b>Waist Circumference§§</b>	76.01 (0.22)	76.42 (0.7)	78.66 (0.22)	77.62 (0.79)	80.94 (0.27)	80.78 (1.08)	82.33 (0.34)	81.6 (0.45)
<b>Body Mass Index##</b>	23.6 (0.1)	24.15 (0.3)	24.37 (0.1)	23.89 (0.34)	24.34 (0.1)	24.69 (0.43)	24.99 (0.14)	24.63 (0.18)
<b>Total Energy Intake***</b>	1262.89 (13.5)	1328.52 (44.36)	1206.11 (13.6)	1236.81 (56.01)	1227.92 (14.03)	1197.08 (62.22)	1106.95 (18.65)	1045.52 (20.68)
<b>Income per Capita†††</b>	0.96 (0.01)	1.02 (0.03)	0.96 (0.01)	1.05 (0.06)	0.95 (0.01)	0.94 (0.04)	1.37 (0.02)	1.35 (0.02)
<b>Urbanization Direction‡‡‡</b>								
no change	126 (7.12)	6 (3.57)	173 (8.9)	4 (3.1)	387 (20.05)	3 (3.85)	77 (6.96)	46 (6.55)
less to more urban	1333 (75.31)	66 (39.29)	1444 (74.32)	67 (51.94)	584 (30.26)	24 (30.77)	806 (72.81)	468 (66.67)
more to less urban	228 (12.88)	60 (35.71)	317 (16.31)	55 (42.64)	958 (49.64)	51 (65.38)	224 (20.23)	188 (26.78)
missing	83 (4.69)	36 (21.43)	9 (0.46)	3 (2.33)	1 (0.05)	--	--	--



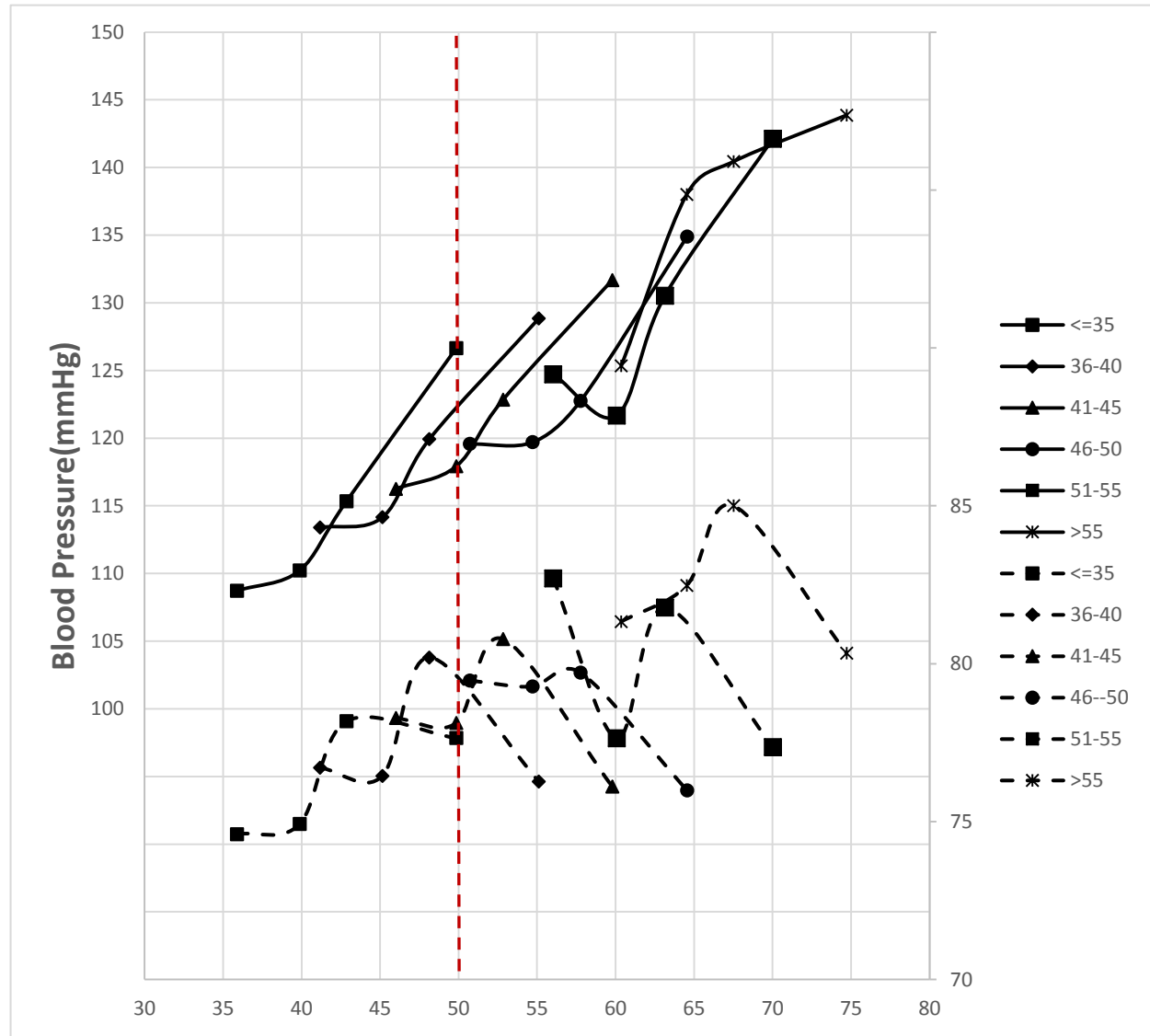
**SUPPLEMENTAL TABLE 4. Longitudinal Characteristics of Non-Movers by Direction of Urbanization from 1998-2012\***

Survey Year	1998			2002			2005			2012		
n†	1938			2072			2008			1818		
	0	+	-	0	+	-	0	+	-	0	+	-
<b>Age‡</b>	42.99 (0.58)	42.01 (0.16)	42.7 (0.43)	45.05 (0.45)	46.12 (0.16)	45.95 (0.35)	48.61 (0.3)	49.01 (0.27)	48.83 (0.19)	55.81 (0.7)	55.89 (0.21)	55.61 (0.39)
<b>Urbanicity Index§</b>	35.08 (1.45)	41.69 (0.33)	24.13 (0.81)	35.58 (1.33)	43.62 (0.34)	34.61 (0.77)	46.67 (0.72)	39.32 (0.52)	38.83 (0.44)	47.27 (1.45)	44.43 (0.42)	47.7 (0.59)
<b>Change in Urbanicity#</b>	0(0)	5.01 (0.07)	-3.34 (0.13)	0 (0)	4.88 (0.08)	-3.83 (0.16)	0(0)	3.91 (0.11)	-3.65 (0.1)	5.9 (0 (0)	-2.75 (0.1)	-2.75 (0.11)
<b>Systolic Blood Pressure**</b>	115.79 (1.69)	113.03 (0.48)	115.05 (1.36)	113.6 (1.52)	114.69 (0.51)	114.09 (1.11)	120.38 (1.04)	119.44 (0.83)	119.38 (0.64)	135.56 (2.93)	129.7 (0.87)	127.98 (1.59)
<b>Diastolic Blood Pressure††</b>	77.58 (1.05)	76.63 (0.32)	77.47 (0.8)	75.76 (0.93)	76.91 (0.33)	75.67 (0.69)	79.5 (0.64)	79.35 (0.51)	79.77 (0.41)	78.94 (1.5)	76.8 (0.45)	75.84 (0.81)
<b>Pulse Pressure‡‡</b>	38.21 (1.02)	36.4 (0.27)	37.58 (0.81)	37.84 (0.92)	37.77 (0.3)	38.42 (0.64)	40.88 (0.7)	40.09 (0.54)	39.61 (0.38)	56.62 (1.94)	52.9 (0.55)	52.14 (1.06)
<b>Waist Circumference§§</b>	74.43 (0.8)	76.36 (0.26)	74.83 (0.63)	77.82 (0.81)	78.83 (0.26)	78.45 (0.54)	81.02 (0.61)	80.62 (0.52)	81.11 (0.37)	81.57 (1.27)	82.28 (0.39)	82.78 (0.8)
<b>Body Mass Index##</b>	22.88 (0.35)	23.8 (0.11)	22.92 (0.29)	23.98 (0.37)	24.4 (0.11)	24.55 (0.23)	24.3 (0.24)	24.24 (0.18)	24.41 (0.14)	24.91 (0.53)	24.93 (0.16)	25.23 (0.33)
<b>Total Energy Intake***</b>	1218.74 (55.83)	1289.57 (15.67)	1171.54 (32.47)	1125.37 (42.9)	1215.31 (15.93)	1211.98 (33.2)	1190.99 (31.29)	1240.97 (25.24)	1235.56 (20.05)	1090.52 (73.48)	1071.1 (20)	1241.57 (50.94)
<b>Income per Capita†††</b>	1.02 (0.04)	0.96 (0.01)	0.92 (0.03)	0.92 (0.03)	0.96 (0.01)	0.96 (0.02)	0.96 (0.02)	0.95 (0.02)	0.95 (0.01)	1.43 (0.06)	1.35 (0.02)	1.4 (0.04)

**SUPPLEMENTAL TABLE 5. Longitudinal Characteristics of Movers by Direction of Urbanization from 1998-2012\***

Survey Year	1998			2002			2005			2012		
n†	1938			2072			2008			1818		
	0	+	-	0	+	-	0	+	-	0	+	-
<b>Age‡</b>	38.56 (1.53)	41.35 (0.66)	41.59 (0.71)	38.48 (2.07)	44.3 (0.64)	44.95 (0.82)	44.7 (4.19)	48.07 (1.21)	46.89 (0.74)	57.91 (1.14)	55.22 (0.27)	54.07 (0.39)
<b>Urbanicity Index§</b>	44.67 (1.91)	44.62 (1.26)	35.52 (1.25)	40 (10.34)	44.52 (1.62)	34.78 (1.46)	50.33 (0.33)	44.75 (2.26)	35.59 (1.55)	41.39 (1.93)	41.69 (0.69)	42.66 (0.81)
<b>Change in Urbanicity#</b>	0 (0)	9.89 (0.89)	-9.42 (0.91)	0 (0)	10.49 (1.11)	-11.22 (1.11)	0 (0)	12.29 (1.97)	-12.37 (1.1)	7.31 (0 (0)	-6.07 (0.24)	(0.49)
<b>Systolic Blood Pressure**</b>	105 (4.28)	115.41 (2.39)	116.22 (2.18)	115.17 (4.68)	114.29 (2.26)	116.19 (2.81)	140.22 (36.3)	120.12 (4.22)	119.18 (1.66)	133.53 (4.06)	129.57 (1.13)	128.03 (1.66)
<b>Diastolic Blood Pressure††</b>	74 (3.27)	76.33 (1.54)	79.58 (1.61)	78.83 (3.76)	76.36 (1.61)	77.67 (1.76)	83.56 (18.19)	81 (2.25)	80.19 (1.1)	79.7 (2.16)	76.76 (0.57)	76.1 (0.91)
<b>Pulse Pressure‡‡</b>	31 (1.91)	39.08 (1.31)	36.64 (1.13)	36.33 (1.99)	37.94 (1.09)	38.52 (1.44)	56.67 (19.16)	39.12 (2.66)	38.99 (1.32)	53.82 (2.55)	52.81 (0.75)	51.92 (0.96)
<b>Waist Circumference§§</b>	74.03 (2.46)	76.63 (1.15)	78.37 (1.13)	82.43 (5.84)	76.97 (1.05)	77.96 (1.27)	83.13 (2.43)	78.91 (1.78)	81.51 (1.42)	79.77 (1.89)	81.09 (0.55)	83.32 (0.86)
<b>Body Mass Index##</b>	23.68 (1.17)	24.28 (0.48)	24.99 (0.5)	25.82 (2.79)	23.49 (0.48)	24.21 (0.5)	26.25 (0.81)	23.92 (0.82)	24.95 (0.54)	24.27 (0.77)	24.37 (0.22)	25.37 (0.35)
<b>Total Energy Intake***</b>	1339.41 (104.82)	1234.36 (55.51)	1388.14 (78.74)	1177.38 (75.69)	1176.05 (61.7)	1282.13 (105.61)	1052.71 (328.35)	1134.66 (77.88)	1234.95 (86.38)	924.23 (83.76)	994.46 (24.26)	1202.3 (41.61)
<b>Income per Capita†††</b>	0.9 (0.07)	1.03 (0.05)	1 (0.05)	0.79 (0.09)	1.02 (0.09)	1.1 (0.07)	0.91 (0.16)	0.83 (0.06)	1 (0.06)	1.36 (0.11)	1.35 (0.03)	1.34 (0.04)

**Supplemental Figure 1. Observed secular trends in SBP\* and DBP from 1998-2012 stratified by baseline age group† among participants with full participation**



\*Blood pressure (BP) was measured from 1998 in triplicate after a 10-minute seated rest using mercury sphygmomanometers. Means were derived from the average of three BP measurements. Solid lines represent SBP and dashed lines DBP. SBP and DBP values are shown on the left and right axis, respectively.

† Based on age when participants first participated from 1998-2012. Every data point represents blood pressure at the mean age within each age group.

## REFERENCES

1. Popkin, B. M., Adair, L. S., & Ng, S. W. (2012). NOW AND THEN: The Global Nutrition Transition: The Pandemic of Obesity in Developing Countries. *Nutrition Reviews*, 70(1), 3–21.
2. Adair LS. Dramatic rise in overweight and obesity in adult Filipino women and risk of hypertension. *Obes Res*. Vol 12, (1335-1341), 2004.
3. Food and Nutrition Research Institute of the Philippines. Emerging Nutrition Concerns: Prevalence of Non-Communicable Disease Risk factors: Time Trends from 1998 to 2015 National Nutrition Survey and Updating of the Nutritional Status of Filipino Children and Other Population Groups. FNRI of the Philippines. 2016 Calabarzon Regional Dissemination Forum; July 28, 2016.
4. Krakoff LR, Gillespie RL, Ferdinand KC, et al. 2014 Hypertension Recommendations From the Eighth Joint National Committee Panel Members Raise Concerns for Elderly Black and Female Populations. *J Am Coll Cardiol*. 2014;64(4):394-402.
5. Okada K, Iso H, Cui R, Inoue M. Pulse pressure is an independent risk factor for stroke among middle-aged Japanese with normal systolic blood pressure : the JPHC study. *Journal of Hypertension*; 29(2):319-324; 2011.
6. Rourke MO, Frohlich ED. Pulse Pressure: Is this a Clinically Useful Risk Factor? *Journal of Hypertension*. 2010;372-374.
7. Domanski M, Mitchell G, Neaton JD, Norman J, Svendsen K. Pulse Pressure and Cardiovascular Disease – Related Mortality. *JAMA*. 2002; 287(20):2677-2683.
8. Thomas F, Blacher J, Benetos A, Safar ME, and Pannier B. Cardiovascular risk as defined in the 2003 European blood pressure classification : the assessment of an additional predictive value of pulse pressure on mortality. *Journal of Hypertension*. 2008, (26): 1072-1077.
9. The International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome. <http://www.idf.org/metabolic-syndrome>. Last accessed on 10/22/2016.
10. Consultation WHOE. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 10 2004;363:157-163.

11. Pereira MA, FitzerGerald SJ, Gregg EW, Joswiak ML, Ryan WJ, Suminski RR, Utter AC, Zmuda JM. A collection of Physical Activity Questionnaires for health-related research. *Med Sci Sports Exerc.* 1997;29:S1-205.
12. Patel A, Huang KC, Janus ED, Gill T, Neal B, Suriyawongpaisal P, Wong E, Woodward M, Stolk RP. Is a single definition of the metabolic syndrome appropriate?--A comparative study of the USA and Asia. *Atherosclerosis.* 2006;184:225-232.
13. Forrest KY, Bunker CH, Kriska AM, Ukoli FA, Huston SL, Markovic N. Physical activity and cardiovascular risk factors in a developing population. *Med Sci Sports Exerc.* 2001;33:1598-1604.
14. FNRI. *Food Composition Tables Recommended for Use in the Philippines. Manila, Philippines: Food and Nutrition Research Institute.;* 1997.
15. Smits, J. & Steendijk, R. The International Wealth Index (IWI). *Social Indicators Research* (2015) 122: 65.
16. Dahly DL, Adair LS. Quantifying the urban environment: a scale measure of urbanicity outperforms the urban-rural dichotomy. *Soc Sci Med.* 2007;64:1407-1419.
17. Office of Population Studies, University of San Carlos; Carolina Population Center, The University of North Carolina at Chapel Hill Nutrition Center of the Philippines. The Cebu Longitudinal Health and Nutrition Survey, Survey Procedures.
18. Tin LL, Beevers DG, and Lip GYH. Systolic vs diastolic blood pressure and the burden of hypertension. *Journal of Human Hypertension* (2002) 16, 147-150.
19. Franklin SS, Larson MG, Khan SA, Wong ND, Leip EP, Kannel WB, and Levy D (2001). Does the Relation of Blood Pressure to Coronary Heart Disease Risk Change With Aging? *Circulation*; 103:1245-1249.
20. Cheng, S., Xanthakis, V., Sullivan, L. M., & Vasan, R. S. (2012). Blood Pressure Tracking Over the Adult Life Course: Patterns and Correlates in the Framingham Heart Study. *Hypertension*, 60(6), 1393–1399.
21. K Kristjansson, JA Sigurdsson, L Lissner, V Sundh, and C Bengtsson. Blood pressure and pulse pressure development in a population sample of women with special reference to basal body mass and distribution of body fat and their changes during 24 years. *International Journal of Obesity* (2003) 27, 128–133

22. Hopstock LA, Bønaa KH, Eggen AE, Grimsgaard S, Jacobsen BK, Løchen M-L, Mathiesen EB, Njølstad I, and Wilsgaard T. Longitudinal and Secular Trends in Blood Pressure Among Women and Men in Birth Cohorts Born Between 1905 and 1977. *Hypertension*. 2015;66:496-501.
  
23. Choh AC, Nahhas RW, Lee M, C YS, Chumlea WC, Duren DL, Czerwinski SA (2011). Secular trends in blood pressure during early-to-middle adulthood: the Fels Longitudinal Study. *Journal of Hypertension*, 29(5), 838–845.
  
24. Goff DC, Howard G, Russell GB, Labarthe DR. Birth cohort evidence of population influences on blood pressure in the United States, 1887–1994. *Ann Epidemiol*. 2001;11:271–279.
  
25. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *JAMA*. 2005;293:1868–1874.
  
26. Kastarinen MJ, Nissinen AM, Vartiainen EA, Jousilahti PJ, Korhonen HJ, Puska PM, Tuomilehto JO. Blood pressure levels and obesity trends in hypertensive and normotensive Finnish population from 1982 to 1997. *J Hypertens*. 2000;18:255–262.
  
27. Attard SM, Herring AH, Zhang B, Du S, Popkin BM, and Gordon-Larsen P. (2015). Associations between age, cohort, and urbanization with systolic and diastolic blood pressure in China: a population-based study across 18 years. *Journal of Hypertension*, 33(5), 948–956.
  
28. Sobngwi E, Mbanya JC, Unwin NC, Porcher R, Kengne AP, Fezeu L, Minkoulou EM, Tournoux C, Gautier JF, Aspray TJ, Alberti K. Exposure over the life course to an urban environment and its relation with obesity, diabetes, and hypertension in rural and urban Cameroon. *International Journal of Epidemiology*. 2004 Aug;33(4):769-76.
  
29. Kinra S, Andersen E, Ben-Shlomo Y, Bowen L, Lyngdoh T, Prabhakaran D, ... for the Indian Migration Study Group. (2011). Association Between Urban Life-Years and Cardiometabolic Risk: The Indian Migration Study. *American Journal of Epidemiology*, 174(2), 154–164.
  
30. Ebrahim, S., Kinra, S., Bowen, L., Andersen, E., Ben-Shlomo, Y., Lyngdoh, T., ... for the Indian Migration Study group. (2010). The Effect of Rural-to-Urban Migration on Obesity and Diabetes in India: A Cross-Sectional Study. *PLoS Medicine*, 7(4).
  
31. Adair, L. S., Popkin, B. M., Akin, J. S., Guilkey, D. K., Gultiano, S., Borja, J., ... Hindin, M. J. (2011). Cohort Profile: The Cebu Longitudinal Health and Nutrition Survey. *International Journal of Epidemiology*, 40(3), 619–625.

32. Vlahov D, Galea S. Urbanization, urbanicity, and health. *J Urban Health*. 2002;79(4 Suppl 1):S1–S12.
33. McDade TW, Adair LS. Defining the “urban” in urbanization and health: a factor analysis approach. *Social Science & Medicine*. 2001;53(1):55–70
34. Van de Poel E, O'Donnell O, Van Doorslaer E. Urbanization and the spread of diseases of affluence in China. *Econ Hum Biol*. 2009;7(2):200–216.
35. Allender S, Wickramasinghe K, Goldacre M, Matthews D, Katulanda P. Quantifying urbanization as a risk factor for noncommunicable disease. *J Urban Health*. 2011;88(5):906–918.
36. Allender S, Lacey B, Webster P, Rayner M, Deepa M, Scarborough P, Arambepola C, Datta M, Mohan V. Level of urbanization and noncommunicable disease risk factors in Tamil Nadu, India. *Bull World Health Organ*. 2010;88(4):297–304.
37. Cyril, S., Oldroyd, J. C., & Renzaho, A. (2013). Urbanisation, urbanicity, and health: a systematic review of the reliability and validity of urbanicity scales. *BMC Public Health*, 13, 513.
38. Okada K, Iso H, Cui R, Inoue M, Tsugane S. Pulse pressure is an independent risk factor for stroke among middle-aged Japanese with normal systolic blood pressure: the JPHC study. *Journal of Hypertension*, 2011 Feb;29(2):319-24.
39. Razak F, Anand SS, Shannon H, et al. Defining obesity cut points in a multiethnic population. *Circulation*. 2007;115:2111–8.